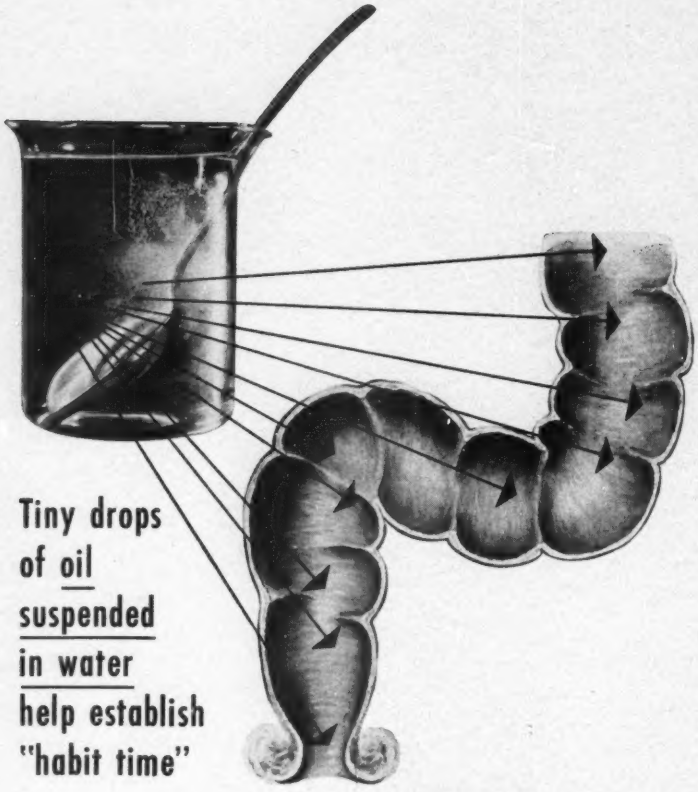
The American Journal of DIGESTIVE DISEASES

An Independent Publication

DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION

ORIGINAL CONTRIBUTIONS

Volume 18 November, 1951 Number 11



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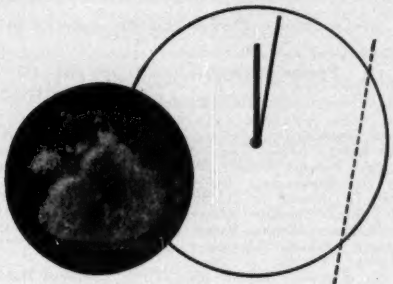

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35 East Wacker Drive
Chicago 1, Illinois

Annual Subscription Rate $6.00; Two Years, $10.00

Single Copies: Current Year 80c. Back Years $1.00.

Editor: Beaumont S. Cornell
Fort Wayne, Indiana

Foreign Subscriptions $7.00; two years $12.00

Regional Editor: Frank J. Lust
17 E. 89th St., New York, N. Y.

Published Monthly at 117 East Main St., Berne, Ind.

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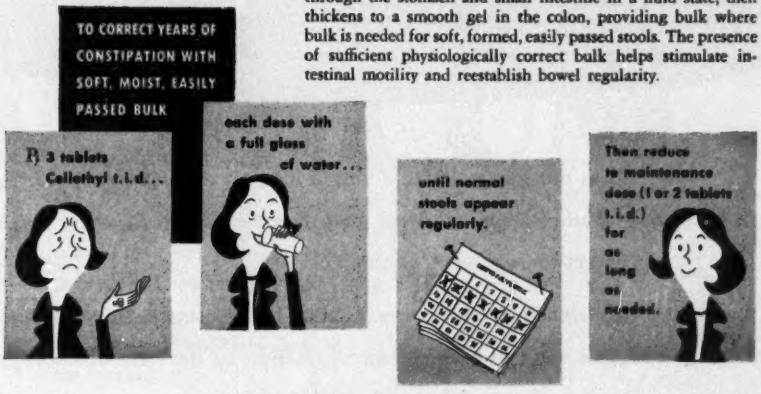

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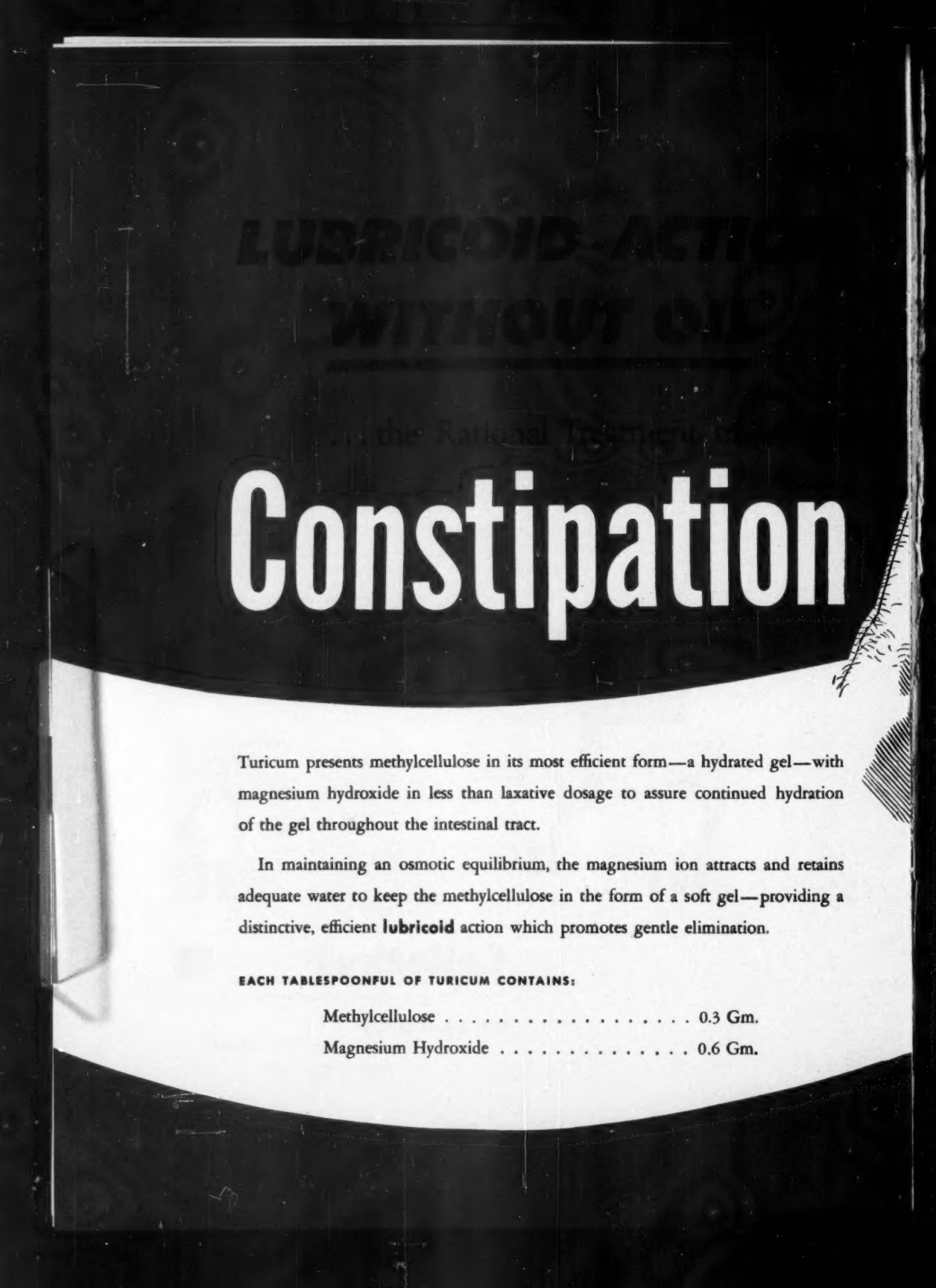

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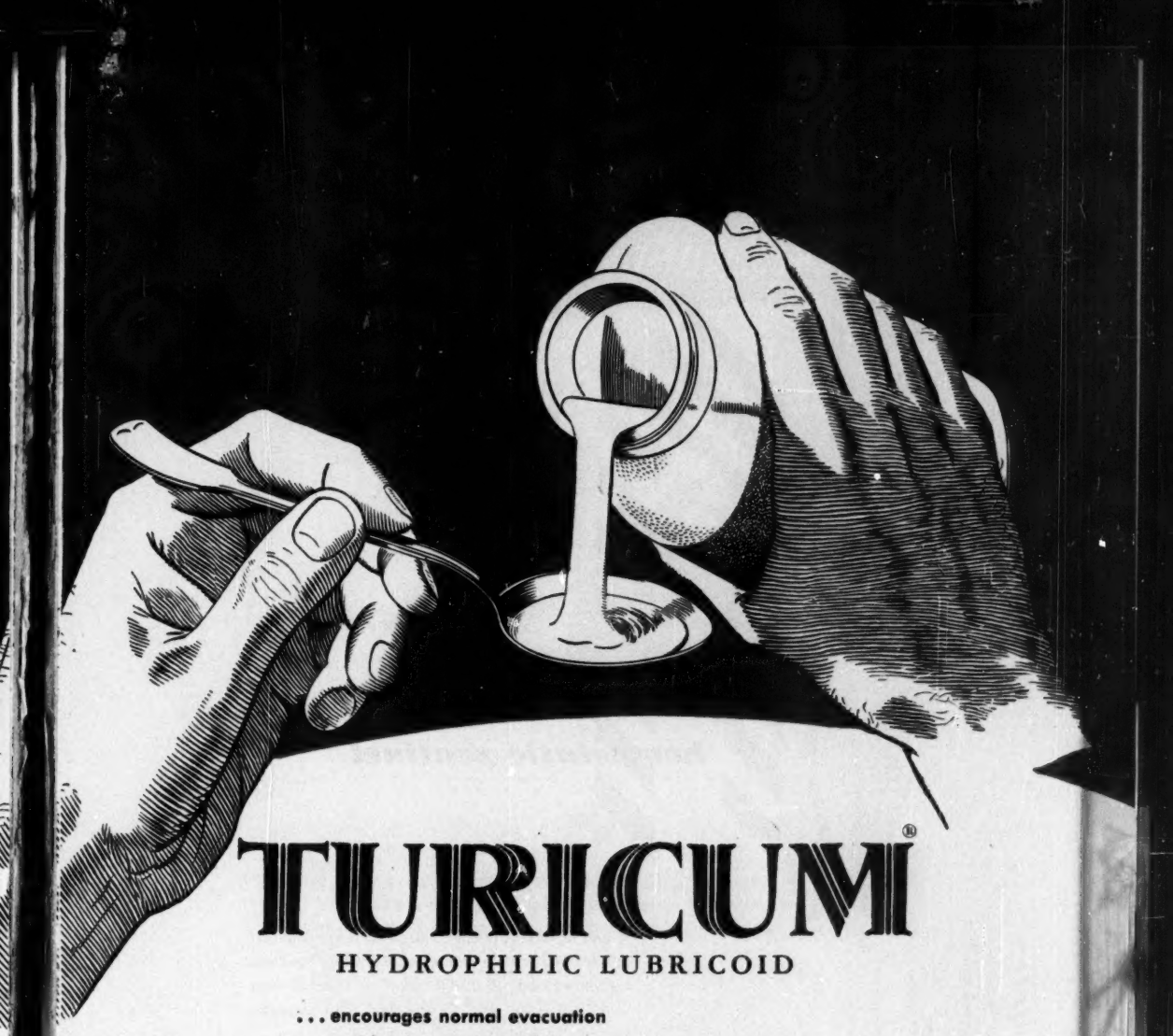

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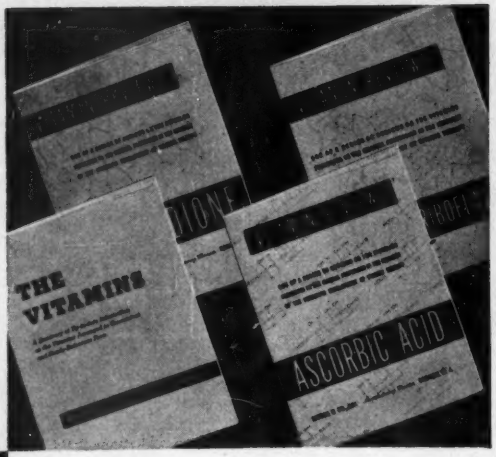

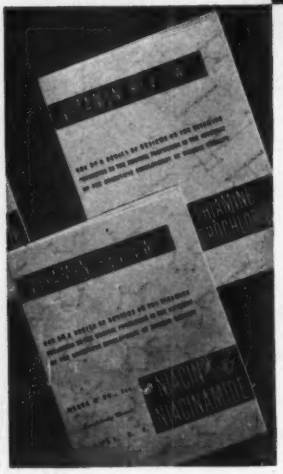

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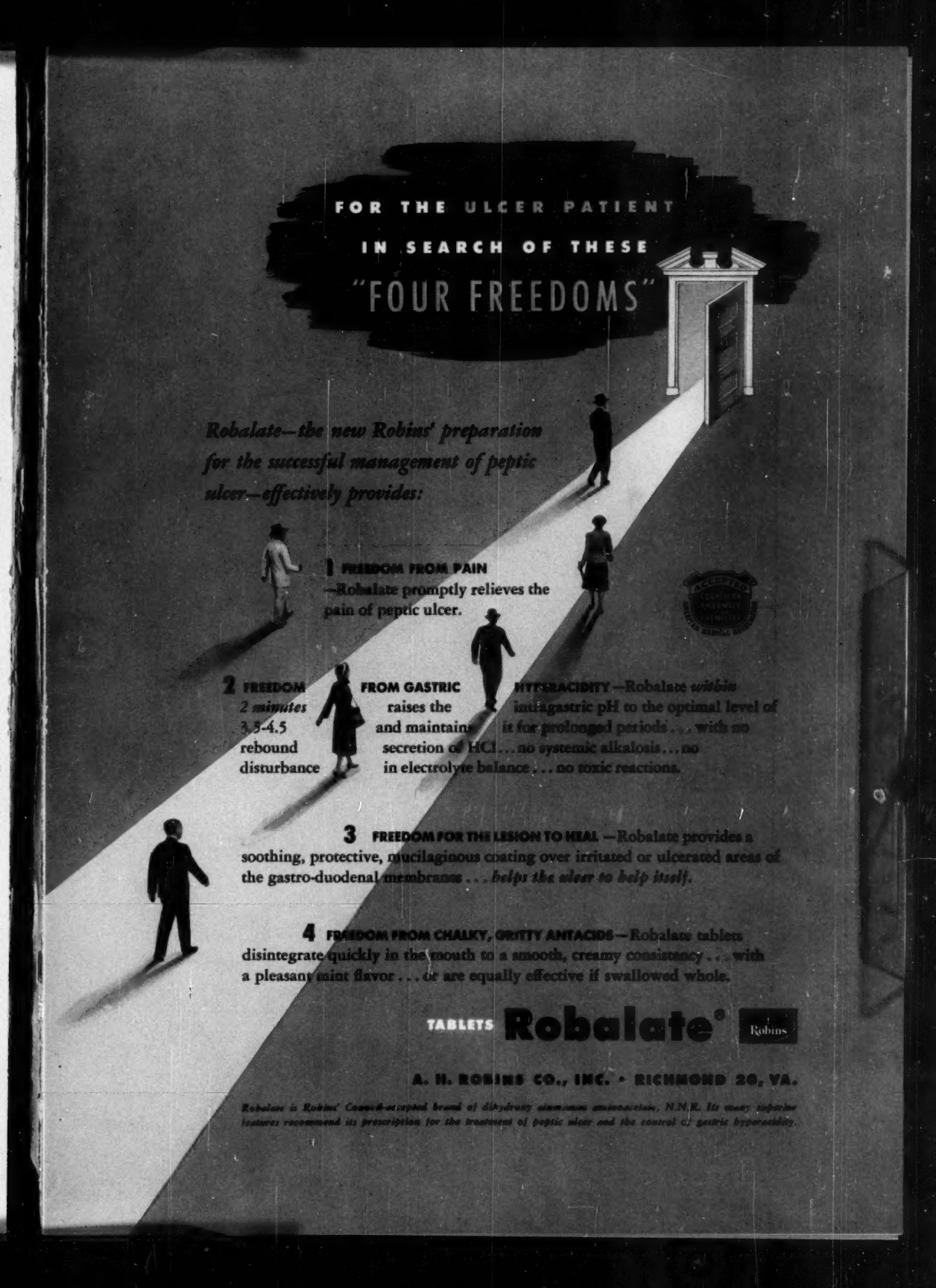
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THE INFLUENCE OF VIRUS HEPATITIS ON THE MORPHOLOGY OF THE GASTRIC MUCOSA

EDDY D. PALMER, MAJOR, M. C.* Washington, D. C.

THERE HAS been much reasonable speculation over a causal association between hepatitis and gastritis, because of the prominence of upper gastrointestinal symptoms during the acute phase of hepatitis. Following convalescence, continuation of a rather characteristic post-hepatitis syndrome in an important proportion of cases has led to assertion that, because liver function tests have returned to normal, it might well be residual stomach disease which is responsible for prolongation of the illness.

The present study was undertaken during a series of investigations into the origins of the chronic gastritides. It seemed necessary to consider hepatitis as a possible cause of acute or chronic mucosal damage. It was thought that the matter could best be studied by making gross observations through the gastroscope and histopathologic observations of biopsied gastric mucosa, at intervals during and following the active phase of virus hepatitis.

MATERIAL

The stomachs of one-hundred patients in various stages (table 1) of either infectious hepatitis or homologous serum jaundice were studied. It happened in 16 instances that the observations were made just prior to the onset of jaundice; in these cases the full clinical picture developed from one to five days later. Most of the other patients were studied during the first eight weeks of the disease. A few were followed for a year. On the basis of clinical, laboratory, and in most cases liver biopsy findings, the cases were divided arbitrarily into three groups to indicate the severity of the hepatitis: 16 patients were considered to have mild hepatitis, 74 moderate, and 10 severe. No case terminated in death. There were nine women and eight Negroes. The ages varied from 18 to 58 years; 88 patients were in the third or fourth decades. All had been hospitalized from the onset of their hepatic illnesses.

It is very difficult to formulate a control group when gastroscopic observations are undergoing evaluation, because patients without stomach complaints or without demonstrated disease which might affect the stomach are ordinarily not gastroscoped. By going over the Gastroscopic Clinic's records carefully, it has been possible to select 100 cases to serve, it is felt, as valid controls. There were six women and 11 Negroes in the group. The ages varied from 17 to 53 years and 78 were in the third and fourth decades. None had upper gastrointestinal complaints, and none had systemic disease which might have influenced the health of the gastric mucosa. Fourteen doctors and nurses were true volunteers. Forty-one patients had been studied in an effort to find suspected retroperitoneal tumors. Thirty-two with metastatic carcinoma had been gastroscoped in a search for the primary tumor site. The others included patients who had had routine gastroscopy following the removal of esophageal foreign bodies, following the repair of penetrating abdominal wounds, and in preparation for certain allergy investigations.

TABLE 1

GASTROSCOPIC FINDINGS IN VIRUS HEPATITIS, IN RELATION TO THE INTERVAL ELAPSING AFTER THE APPEARANCE OF THE FIRST SIGNIFICANT SYMPTOM

Weeks after onset first symptom	No. cases	Gastroscopic findings			
		Normal	Chronic superficial gastritis	Chronic atrophic gastritis	Chronic hypertrophic gastritis
1	16*	12		1	3
	13**	12	1		
2	16	14			2
3	12	8		1	3
4	12	10	2		
5-8	20	18	1		1
9-16	7	7			
17-52	4	3	1		
Totals	100	84	5	2	9

*Before onset of clinical jaundice.
**After onset of clinical jaundice.

METHODS

The observations were based on the gastroscopic appearances and the histopathologic examination of tissue removed from the gastric mucosa just prior to gastroscopy. All patients and control subjects were gastroscoped, 40 of them more than once. Mucosal tissue was taken from 25 hepatitis patients and was available in 22 of the control group. The tissue specimens were removed blindly from the pars media with the vacuum tube (12), were fixed immediately, and stained with hematoxylin and eosin.

RESULTS

It happened that positive stomach findings in this series and in the controls were confined to the gastritides; no incidental ulcers or tumors were encountered.

A summary of the gastroscopic observations is presented in tables 1 and 2. Abnormal mucosa was encountered in 16 hepatitis patients; in nine the disease was chronic hypertrophic gastritis, in five chronic super-

TABLE 2

COMPARISON OF THE GASTROSCOPIC FINDINGS AMONG THE HEPATITIS AND THE CONTROL PATIENTS

	No. cases	Normal	Chronic gastritis		
			Superficial	Atrophic	Hypertrophic
Hepatitis patients	100	84	5	2	9
Controls	100	88	3	5	4

Submitted June 12, 1951.

*From the Gastrointestinal Section, Walter Reed Army Hospital, Washington, D. C.

ficial gastritis, and in two chronic atrophic gastritis. It was found that there was no correlation between the type or severity of the gastritis and the stage of the hepatitis. Furthermore, when the clinical severity of the hepatitis was compared with the incidence of positive stomach findings, no correlation was apparent. Chronic gastritis was present in 12 of the control patients, and the three major types were represented in approximately equal proportions (table 2).

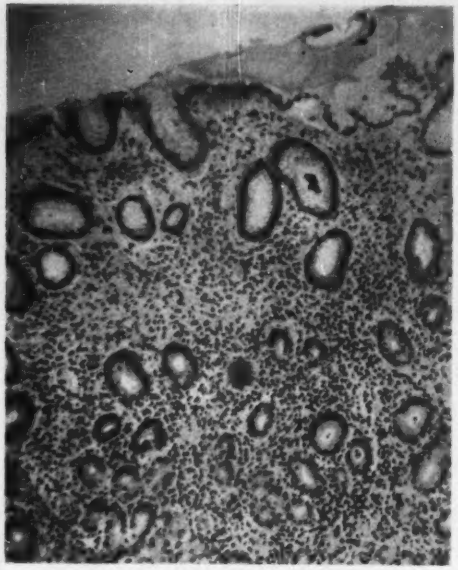

Fig. 1: Tissue removed during the second week of illness. The foveolar layer is moderately infiltrated with lymphocytes. The foveolae are widely separated by severe subsurface edema.

Among the hepatitis patients, 22 of the 25 biopsied mucosal specimens were considered to be normal (table 3). In one patient, biopsied during the second week of illness, the foveolar layer was markedly edematous and moderately infiltrated with round cells (fig. 1). The cellular exudate was composed almost entirely of lymphocytes, with only an occasional eosinophil and plasma cell. The foveolae were widely separated by the edema. In two instances prominent necrobiosis was found at the junction of gland and foveola, characterized by focal necrosis and evidence of glandular cell regeneration (figs. 2, 3). One of these latter two biopsies

TABLE 3

GASTRIC MUCOSAL BIOPSY FINDINGS AMONG HEPATITIS PATIENTS

Weeks after onset first symptom	No. cases	Findings		
		Normal	Necrobiosis	Excess round cell infiltration
1	5	4	1	
2	4	3		1
4	2	2		
5-8	8	8		
9-16	6	5	1	

Fig. 2: Necrobiosis in region of foveolar-glandular junction. There are both focal cellular necrosis and evidence of glandular cell regeneration.

was taken during the first week of the disease and the other during the tenth. The foveolae of the latter (fig. 3) were filled with extruded glandular cells, on their way towards the gastric lumen.

Among the control group, too, two instances of necrobiosis of the neck region were encountered, and in one case, which had been diagnosed gastroscopically as chronic hypertrophic gastritis, prominent increase in the thickness of the foveolar layer was found (table 4).

DISCUSSION

Prominence of anorexia, nausea, vomiting and cramping pain during the early phase of acute infectious hepatitis has suggested to many observers that causally related gastritis may accompany the basic disease, perhaps as a regular feature of the over-all picture. In some of the acute infectious diseases which are produced by organisms with notably toxic powers, such as diphtheria and scarlet fever, the gastric mucosa reflects local insult by an acute gastritis. Although infectious hepatitis has no such toxic feature, the thought has been expressed from time to time that an inflamed liver may not be able to detoxify certain circulating endogenous metabolic products, which then might injure susceptible tissues, including the gastric mucosa. Wichels and Brinck (16), in a rather remarkable series of papers, made some interesting postulations—some shrewd, some fanciful—regarding the interrelationships between these noxious agents, the stomach, and hepatobiliary disease. They pointed out that poisons which have an elective effect on the liver often seem as well to produce gastritis. They

TABLE 4

COMPARISON OF BIOPSY FINDINGS AMONG HEPATITIS AND CONTROL PATIENTS

	No. patients	Normal	Necrobiosis	Excess round cell infiltration	Foveolar hypertrophy
Hepatitis	25	22	2	1	0
Control	22	19	2	0	1

believed that the stomach damage, first manifested by secretory depression and later by morphologic changes, is due to inability of an injured liver to clear the blood of circulating toxic elements, whether these elements be exogenous or endogenous. Liver damage produced in dogs by clamping the common duct, for instance, was followed by gastric mucosal fibrosis.

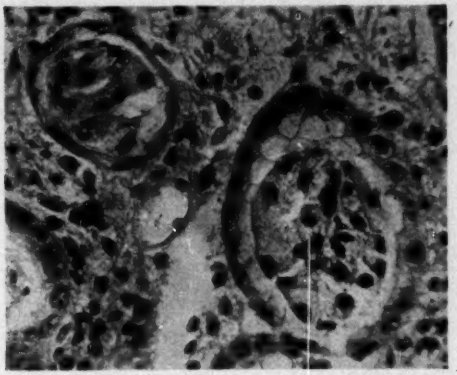

Fig. 3: These foveolae are filled with extruded glandular cells, close to areas of necrobiosis.

The results of objective clinical studies, however, have not served to confirm a correlation between hepatic and gastric disease. By combining the results of several gastroscopic studies, including the present one, made during the acute phase of hepatitis, it is found that among 137 patients there were only 17 instances of chronic superficial or erosive gastritis, three of atrophic gastritis, and nine of hypertrophic gastritis (1, 6, 8, 9). One might expect that mucosal petechiae would be common, in view of the thrombopenia and increased capillary fragility which frequently accompany liver disease (15), but this is not so. In general, the gastroscopists have found nothing which could be considered contributory to the gastric symptoms of the patient with acute hepatitis (1, 9). The findings of Knight and Cogwell (8) and Havens and associates (6) were suggestive of an association, but their series were very small. The results of the biopsy studies presented herein prove rather well that the gastric mucosa in the great majority of cases of acute infectious hepatitis shows no microscopic abnormality.

Perhaps morphologic evidences of damage become manifest only after a longer lapse of time than that covered by the present study. In chronic liver diseases which appear to be sequelae of acute hepatitis, however, it is difficult to arrive at a satisfactory conclusion regarding causal relations of observed gastric abnormalities. Raby and Wanscher (13) made careful histopathologic studies of 110 patients who had died with various combinations of chronic liver and stomach diseases, but found it impossible to offer convincing proof that either was directly responsible for the other. Cox (3) in a similar autopsy study, observed microscopic evidence of gastritis in 19 of 43 patients with portal cirrhosis, but found even more gastritis in the absence of liver disease among a similar number of control autopsies. He concluded, ". . . liver cirrhosis and the conditions which lead to it do not produce chronic atrophic gastritis."

When the problem is approached from the other direction, it is found that there may be a certain incidence correlation between some primary gastric and duodenal diseases and hepatic dysfunction, but that most of it appears to be merely coincidental. Most striking was Morrison's (10) observation that among 50 peptic ulcer patients there was evidence of substandard liver function in 36. Khurgin (7) postulated that gastric exocrine deficiency must necessarily have a deleterious nutritional effect on the liver, but one must suppose that any such effect is merely one of degree and is of little practical importance. Zemets and Esina (17) and Evard (5) have described several cases of gastritis with decreased liver function, but these were collected instances and smacked of mere coincidence. In the same category belong the cases of gastric and duodenal ulcer associated with hepatic disease described by Barker and Capps (2) and Oliver Pascual and colleagues (11). Historically, it is interesting to note that in 1865 Virchow observed at autopsy in a case or two of hepatitis that the orifice of the common duct was obstructed by a plug of mucus; the result of a chance observation plus the tremendous medical stature of Virchow was an immediate wide-spread acceptance of gastroduodenitis as the cause of hepatitis, or "icterus gastro-duodenalis." This interesting episode has been editorialized as ". . . a sad illustration of man's unreasoning acceptance of authority. . ." (4).

CONCLUSION

Gastroscopic investigation of 100 patients with acute virus hepatitis, and microscopic study of gastric mucosa removed by biopsy in 25 revealed no more disease than was found in a similar number of control subjects. It is concluded that the morphology of the gastric mucosa is not affected adversely during acute virus hepatitis.

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HEREDITY AND DIABETES*

E. M. Watson, M.D., M.Sc., F.A.C.P.** and Margaret W. Thompson, B.A., Ph.D.***
London, Canada.

"DIABETES IS AN hereditary disease, characterized by an increase of glucose in the blood and the excretion of this sugar in the urine; it is dependent upon the deficient formation or diminished effectiveness of insulin secreted by the islands of Langerhans of the pancreas and is functionally interrelated with conditions arising in the liver and in endocrine glands other than the pancreas, particularly the pituitary, but also the adrenal and thyroid" (Joslin, 1).

This concise and comprehensive definition of diabetes mellitus by a lifelong student of the disease serves to emphasize that most, if not all, examples of diabetes in man involve more than a mere lack of insulin secretion. The evidence points to the implication of several probable etiological factors which operate singly or in various combinations to bring about the diabetic syndrome.

The Significance of Heredity

Actually, we know much more about the methods by which diabetes can be produced experimentally in animals than we know about the causes of clinical diabetes mellitus. Experimental diabetes is not necessarily the same condition as clinical diabetes. One distinguishing feature is a pronounced inherited susceptibility to the development of the clinical form of the disease.

The commonly observed high incidence of diabetes in the immediate relatives of diabetic patients and the coincidental occurrence of the malady in uniovular twins constitute simple supportive evidence of the etiological significance of heredity. With the prolongation of the lives of young diabetics to a stage of normal fecundity, the incidence of familial diabetes promises to become even more impressive than it is at the present time. Also, with the protracted observation of the members of diabetic families, along with the conduct of mass surveys of the population for the detection of diabetics, doubtless the true mode of the inheritance of this disease eventually will evolve.

It is not known with any degree of certainty whether or not all cases of diabetes possess a genetical basis or, if they do so, that this is identical in every instance. Nevertheless, the genetical uniformity of the condition may be assumed as a working hypothesis. Evidence favoring its uniformity is provided by the observation that the longer a series of diabetic patients is observed, the higher does the percentage of familial cases become. It is quite conceivable that, if sufficient accurate information were obtainable, a positive family history of diabetes might be traced for every true diabetic.

Submitted May 15, 1951.

*From the Department of Pathological Chemistry, Faculty of Medicine, University of Western Ontario and the Diabetic Service, Victoria Hospital; aided by a grant from the National Research Council of Canada.

**Professor of Pathological Chemistry and Senior Associate in Medicine.

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The Genetics of Diabetes

The genetics of diabetes presents a complex problem. It has not been possible as yet to postulate for this disease the kind of precise gene-effect relationship that obtains for certain other metabolic disorders, for example, alkaptonuria. If diabetes be always hereditary, certain possibilities such as the involvement of an allelic series rather than a single pair of genes; or different genes that affect different aspects of the carbohydrate metabolism; or secondary, inherited factors influencing the onset age and the severity of the disease represent aspects of the problem which invite further inquiry from the genetical point of view.

The pattern of heredity in diabetes is complicated also by the influence of "extrinsic" or "inciting" etiological factors. For some inheritable qualities, the best known of which probably are the various blood types, the inherited potentiality (genotype) is expressed in a uniform manner regardless of accessory or environmental effects but in the majority of hereditary conditions, including diabetes, environment in the broadest sense of the term, as well as heredity, determines the "penetrance" or "expressivity" of the genotype. Snyder (2) defines penetrance as "a statistical concept of the regularity with which a gene produces its effect" with the further remark that "when the manifestations of a trait produced by a gene are different from person to person, we say the gene has variable expressivity." The clinical "expression" (phenotype) of diabetes may appear at any age and has a wide range of severity. Therefore, many individuals possessing the diabetic genotype may escape recognition because they expire before the condition has revealed itself or, due to the subclinical nature of the disease, a diagnosis of diabetes is never established. Thus the absence of full concordance between genotype and phenotype is the chief reason why the mode of inheritance of diabetes lacks clarification.

The Investigation

Approximately 46 per cent of 1,222 diabetic patients observed at the Victoria Hospital, London, Ontario, between 1934 and 1944 showed a positive family history of diabetes. *i.e.* each patient possessed at least one known diabetic relative (3). A similar survey completed in 1950 and embracing 1,380 persons, some of whom were included in the earlier investigation, gave an incidence of positive family histories of 50 per cent (4). A control group of non-diabetic individuals of comparable age and sex gave a positive family history of diabetes in only 14 per cent. These findings are in essential agreement with those of other observers. For example, Wilkerson and Krall (5) found for a series of 3,516 persons that 38.6 per cent of the adult

diabetics and 18.2 per cent of the non-diabetics presented family histories of diabetes.

The incidence of cases of diabetes with known positive diabetic family histories varies, apparently, with the age at onset of the disease. As previously reported (4), the percentage of patients with a known positive family history fell gradually from 79 per cent in those with onset of their diabetes in the first decade of life, to 26 per cent in those with onset in the ninth decade. The only exception to the general trend was in the second decade, where the percentage of positive family histories was found to be unexpectedly low, particularly for the females, but this discrepancy may be apparent rather than real owing to the comparatively small number of patients encountered in this onset age group. Similar observations have been reported by Munro, Eaton and Glen (6).

An association between heredity and age at onset was further indicated by reason of the fact that the mean age at onset was lower in those patients with a positive, particularly a bilateral positive, family history of diabetes than in those with no diabetic kindred. These observations suggest the greater relative importance of heredity, as opposed to other etiological influences, in the cases where the disease manifests itself at an early age in contrast to those with its onset later in life.

Many of the earlier studies of the inheritance of diabetes are of little value from the standpoint of genetical analysis. For example, Cammidge (7) regarded as examples of dominant inheritance those cases in which the disease had appeared in an antecedent of the propositus (the individual who brings a pedigree to notice initially) and as recessive those in which sibs were affected. The same distinction between "hereditary" (dominant) and "familial" (recessive) inheritance is drawn in many clinical reports but such data are of very limited value in determining the true mode of transmission of any disorder.

Allan (8), Allen and Mitchell (9), Burnstein and Patterson (10), Kennedy (11), Wright (12) and many others have described pedigrees of diabetics which, when considered as a whole, further emphasize the fact that the mode of inheritance of diabetes lacks specification. It is well known that individual pedigrees can be misleading and probably the most significant deduction emerging from such records is the desirability of long-term, careful surveys of the relatives of the diabetic population, covering several succeeding generations.

Pincus and White (13) reviewed the family histories of 523 diabetic patients and found the incidence of diabetes to be significantly higher than in the families of 153 non-diabetics. Assuming recessive inheritance as the simplest hypothesis, they found reasonably close agreement between observed and expected numbers of diabetic sibs of propositi when the cases were classified as to the presence or absence of diabetes in the parents and when allowance was made for the variability of the onset age. They concluded that diabetes was inherited as a Mendelian recessive trait.

At about the same time Levit and Pessikova (14) reported upon a series of 258 diabetic families. Their paper evidently is the source of the statement appearing in certain textbooks of medical genetics (*e.g.* Snyder, 15; Crew, 16; Muller *et al*, 2), to the effect that diabetes is inherited as a dominant with 10 per cent "penetrance." Because of the language difficulty, the original paper probably will have been studied by comparatively few individuals interested in the subject. However, a reassessment of the findings of Levit and Pessikova permits a ready refutation of their argument against the recessive inheritance of diabetes and indicates also flaws in their argument for dominant inheritance. Consequently, their conclusions can not be accepted unreservedly.

Evidence for Recessive Inheritance. More recent studies of the genetics of diabetes include those of Hanhart (17, 18), who has prepared extensive pedigrees, some of which extend back for seven generations. Thus he has been able to confirm the existence of consanguinity in the parents of several of his diabetic propositi. One is unable to judge, however, whether the incidence of cousin marriages is extraordinary or not for the particular population groups studied, namely, the inhabitants of isolated Swiss cantons. Hanhart regards the mode of inheritance to be recessive and his pedigrees support this view.

Harris (19, 20) has recently analyzed in detail the family histories of 1,241 diabetic propositi and noted an unusually high rate of parental consanguinity among those cases with onset of the diabetes before the age of 30 years but not in those with a later onset age. He demonstrated that the age at onset was positively correlated in diabetic sib pairs but not, or only slightly, correlated in parent-child pairs. He propounded the hypothesis that the early onset form of diabetes represents the homozygous and the late onset form the heterozygous condition but his papers to date do not test this hypothesis which, indeed, would appear very difficult to test.

Steinberg and Wilder (21) have reported the frequency of diabetes among the sibs of diabetic patients to be approximately six per cent when neither parent was diabetic and 12 per cent when one parent was diabetic. The ratio of these frequencies is 1:2, which ratio would be expected if the inheritance is recessive.

In a general investigation of the genetics of diabetes mellitus, the present writers found the incidence of diabetes in the sibs of diabetic propositi to be 7.69 per cent when neither parent was diabetic and 15.30 per cent when one parent was affected (see Table 1). These figures which are in the ratio of 1:1.99 agree with the ratio obtained by Steinberg and Wilder (21) and, furthermore, are in accord with hypothesis of recessive inheritance. Only four of the propositi had both parents affected and for these the incidence of diabetes in the sibs was but 8.33 per cent. Admittedly, this figure is lower than expected, but no conclusions can be drawn from so small a series of cases.

TABLE I

THE INCIDENCE OF DIABETES AMONG THE SIBS OF DIABETIC PROPOSITI CLASSIFIED BY THE PHENOTYPES OF THE PARENTS

Parents	Total number of sibs	Number of diabetic sibs	Incidence of diabetes in the sibs
Neither diabetic	3836	295	7.69%
One diabetic	771	118	15.30%
Both diabetic	24	2	8.33%
Total	4631	415	8.96%

Sex-Linked Factors. The observations of Penrose and Watson (3) suggested that pairs of diabetic brothers and pairs of diabetic sisters occurred more frequently than diabetic brother-sister pairs. This was regarded as evidence for the operation of secondary, sex-linked modifying genes. Harris (22) reported the same tendency among the sibs of his series. However, in the present investigation, when the expected proportions were calculated on the basis of the sex ratio obtaining among the propositi (40.5 per cent males; 59.5 per cent females), the excess of like-sexed pairs was found to be statistically insignificant (see Table II). Consequently, for the present series, the apparent tendency for diabetes to occur with greater frequency in the like-sexed than in the unlike-sexed sibs of the propositi can be fully explained on the basis that more females than males exhibit diabetes mellitus.

TABLE II

OBSERVED AND EXPECTED NUMBERS OF DIABETIC SIB PAIRS CLASSIFIED ACCORDING TO SEX

Type of sib pair	Number of pairs observed	Number of pairs expected
Brother-brother	95	79.87
Brother-sister	217	234.73
Sister-sister	175	172.40
Like-sexed	270	252
Unlike-sexed	217	235
Total	487	487

$X^2 = 2.655$ $n = 1$ $P = 0.10\text{-}0.20$

PRACTICAL CONSIDERATIONS

While the theoretical aspects of the inheritability of diabetes are of great interest to the student of human genetics, the wholly practical aspects of the subject are the concern of the clinician and a considerable number of his diabetic patients. Not infrequently, the physician is requested to impart information regarding the likelihood of the development of diabetes in the offspring or other kin of those afflicted with the disease.

Reliable and enlightening observational data bearing upon this matter are difficult to obtain and to assess, chiefly because a time lag, often of many years' duration, usually exists between the manifestation of diabetes in the parent and in the offspring.

The theoretical proportion of affected progeny, on the hypothesis that diabetes is inherited as a Mendelian recessive trait, may be stated as follows: For any recessive trait, the proportion of affected offspring depends upon the genetic constitution of the parents. If both parents are affected, 100 per cent of the offspring can be expected to show the trait; if one parent is affected and the other unaffected but is a "carrier" (in genetical language, a heterozygote), 50 per cent of the progeny will be affected; and if one parent is affected and the other "normal" (*i.e.* completely free of the gene), none of the offspring will be affected though all will be carriers, capable of transmitting the trait to their progeny if they marry affected persons or other carriers.

Owing to the frequent paucity of desirable medical information concerning patients' ancestors and because full concordance between genotype and phenotype is lacking in diabetes, it is not possible, usually, to determine with certainty the genetic constitution of the connubial partners of diabetic individuals. This adds to the difficulty of predicting whether or not the descendants of a particular union will be diabetically disposed.

For the present series, since the genotypes of the marriage partners could not be ascertained, the children of the diabetic propositi were classified by the phenotype and family history of the spouse, *i.e.* whether he or she was: (a) non-diabetic and of a non-diabetic family; (b) non-diabetic but with a positive family history of diabetes or, (c) diabetic. The proportion of diabetic offspring was calculated for each group, as shown in Table III.

TABLE III

THE INCIDENCE OF DIABETES AMONG THE OFFSPRING OF DIABETIC PROPOSITI CLASSIFIED BY THE PHENOTYPE AND FAMILY HISTORY OF THE SPOUSE

Conjugal combinations	Total number of offspring	Number of diabetic offspring	Incidence of diabetes in offspring
Spouse non-diabetic; family history negative.	2530	48	0.90%
Spouse non-diabetic; family history positive.	118	8	6.78%
Spouse diabetic.	99	3	3.03%
Total	2747	59	2.15%

Because the mean age of the offspring included in Table III is well below the mean age at onset of diabetes in general it is expected that a larger proportion than indicated will eventually become diabetic. Consequently, the percentages of affected offspring shown in the Table must not be interpreted as an indication of the number of potentially diabetic individuals in the series. It will be necessary to review the groups from time to time in order to gain more conclusive information. It is notable, however, that the percentage of affected offspring is markedly higher when the spouse is diabetic and/or a member of a diabetic family (*i.e.* when the offspring have a bilateral diabetic family history) than when the spouse is non-diabetic and of a family in which no diabetes is known (*i.e.* when the offspring have a unilateral diabetic family history).

Obviously, the observed number of diabetic progeny of diabetic parents falls far short of the theoretical computations. Admittedly, the exactness of the data herein reported would have been enhanced had glucose tolerance tests been performed on all of the individuals in the several groups who were not obviously diabetic. Despite the fact that expected genetical ratios are incapable of fulfillment for several reasons, the findings attest the inadvisability, realized by many physicians and patients alike, of the marriage of two diabetics or the marriage of a diabetic and a non-diabetic member of a family in which diabetes exists or has existed.

CONGENITAL DIABETES

Schwartzman, Crusius and Beirne (23) have discussed cases of diabetes with onset of the malady during the first year of life. Cases of this kind constitute 0.5 per cent of all diabetic children, who in turn represent about five per cent of the total diabetic population. To the geneticist, the very young juvenile diabetics

are of especial interest because, presumably, a minimal "environmental" and a maximal "genetic" component are operative. A positive family history of diabetes was obtained in 12 of 28 of their cases (43 per cent). A circumstance upon which the authors did not comment, however, is that three of the four congenital diabetics listed in their review were born of diabetic mothers. If this association is not merely fortuitous, it would be of interest to know its basis. It is conceivable that *maternal hyperglycaemia*, especially if persistent, may be the factor responsible for the antenatal metabolic breakdown in the hereditarily predisposed foetus.

THE PHENOMENON OF ANTICIPATION

The phenomenon of "anticipation," *i.e.* the tendency for a disease to appear at an earlier age in successive generations, has received some attention with respect to diabetes. Several authors (*e.g.* Burnstein and Patterson, 10) have described this feature, with the publication of pedigrees that appear to support it. Stern (24), in a general discussion of anticipation, pointed out that since a serious disease which affects persons early in life reduces their chances of producing offspring, selection operates against potential pedigrees with early onset of the disease in an older generation and thus only the individuals of the older generation with later onset remain available for the records. A similar explanation concerning the question of anticipation in diabetes had been given previously by Levit and Pessikova (14). More recently, Steinberg and Wilder (25) showed that the apparent tendency for diabetes to develop at an earlier age in successive generations is due to unavoidable errors in sampling and that, by chance alone, 65.3 per cent of their cases would have had an earlier onset than their affected parents, whereas 70 per cent of the pertinent family histories actually exhibited such anticipation. They proposed, therefore, that the term be dropped with respect to diabetes.

DISCUSSION

With the assumption, based upon a substantial bulk of evidence, that the appearance of diabetes in an individual, especially during childhood or youth, is the fruit of a family diabetes that has already existed in one or more previous generations, it is logical to consider what inherited characteristic or characteristics account for, or are associated with, the familial tendency toward the disease. In this regard, the pancreas comes to mind as the organ most likely to be involved. However, anything of the nature of proof of inherited pancreatic deficiency is sadly lacking, although there is some indication that the size of the pancreas, on the basis of pancreas: body weight ratios, is abnormally small in young diabetics.

Of course, it is quite conceivable that certain individuals are born with an inadequate number of pancreatic islets which sooner or later succumb to the effects of metabolic stress. So far, however, studies of the number and size of the islands of Langerhans seem to add nothing to our understanding of the hereditary defect.

Reverting to the comparative physiology of diabetes, it has been observed that normal animals, even of the same species, exhibit considerable variability in the ease with which they become permanently diabetic by means of the various diabetogenic agents. The resistance of these animals appears to be related not to their body weight or gross pancreatic weight but to the size of what, for want of a better name, is referred to as their insular reserve capacity. As a corollary, it seems reasonable to suppose that man, the most variable of animals, possesses similar inherent variations in his resistance to the processes which tax his insular function, even although such deviations can not be expressed in terms of any measurable biological standards. Apparently, in some individuals, the metabolic processes are capable of surviving conditions which destroy those of others.

Next to the pancreas, the pituitary and the adrenal glands are the endocrine organs most concerned with the control of sugar metabolism. Evidence might be cited indicating that the nature of the pituitary functions may be an inheritable quality related to certain racial as well as familial characteristics.

Even although the subject of carbohydrate metabolism has undergone revolutionary developments during the past two decades, we are still groping in the darkness with respect to many of the problems relating to diabetes mellitus and its major complications. Light will come with a fuller knowledge of the tissue-enzyme systems, with further information concerning hormones other than insulin; also the rôle of the lipids in chemical pathology and with the elucidation of additional, but as yet undiscovered factors, including the genetical influences which undoubtedly affect the metabolic processes.

SUMMARY

Although diabetes mellitus shows a marked familial tendency, the exact mode of inheritance of the disease, as yet, has not been determined completely, chiefly because of the absence of full concordance between the diabetic genotype and phenotype. The percentage of cases with positive family histories of diabetes varies inversely with the age at onset of the disease. The age at onset is earlier in those cases with positive family histories of diabetes than in those without such family histories and is especially early in those with bilateral family histories. On the whole, the available evidence favors the hypothesis that diabetes is inherited as a recessive. The age at onset of the disease is positively correlated in sibs but not, or only slightly, correlated in parent-offspring pairs. There is conflicting evidence as to whether diabetes is more likely to appear in the like-sexed than in the unlike-sexed sibs of diabetic propositi, but the present observations suggest that if any such relationship exists, it can be explained on the basis of the preponderance of female diabetics.

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EVALUATION OF CLINICAL METHODS IN GASTRO-INTESTINAL DISEASE. IV. AUTOPSY FINDINGS OF LIVER DISEASE (FATTY INFILTRATION, HEPATIC CIRRHOSIS) OBSERVED IN PEPTIC ULCER CASES

A. ALLEN GOLDBLOOM, M. D., F. A. C. P., ABRAHAM LIEBERSON, M. D., F. A. C. P. AND AARON SILVER, M. D., A. A. C. P. New York, N. Y.

THERE HAVE been reports in the literature, increasingly so lately, of liver disease produced by peptic ulcer. Budd (1) described in 1855 a case of hepatic cirrhosis in association with gastric ulcer. MacCarty (2) quotes Meyer, Maffuci and Tsunoda who as long ago as 1872 (and again in 1876, 1882 and 1908) produced experimental biliary cirrhosis by a partial stenosis of the common bile duct,—a surgical condition often caused by duodenal ulcer. MacCarty mentions the possible relation of duodenal ulcer to hepatic cirrhosis. Its incidence in connection with cirrhosis was found to be 2% or less by Hauser (3) in an autopsy series. In Schnitker and Haas' review (4) of 72 autopsy cases showing advanced liver cirrhosis there were 14 (20%) who coincidentally exhibited peptic ulcer. They considered the results of their study to be inconclusive, however, and felt that the liver disturbance was probably functional in nature. The observers who have found the closest relationships between liver damage and peptic ulcer are Mateer and his associates (5). They studied 132 cases of cholelithiasis and 31 peptic ulcer (operative cases) by combined liver biopsy and liver function study. Of the 31 ulcer cases they found only two with completely normal livers. This is a subject that bears a lot of investigation,—for if there is a causal relationship between peptic ulcer and chronic liver disease it behooves us clinicians to institute a rigid prophylactic regime in treating peptic ulcer that would prevent chonic, irreversible liver damage.

In previous publications (6, 7, 8) on this subject we have shown that there is no cholesterol disturbance in peptic ulcer patients, likewise liver function tests were within normal range, particularly in patients with uncomplicated peptic ulcer (7). To investigate the possibility that there may be pathological liver changes present even while the liver function tests were normal, we felt it worth while to review the autopsy reports of patients in which the pathological diagnosis of peptic ulcer was made,

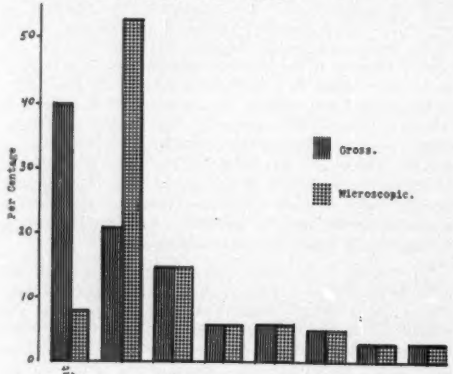

Fig. 1: Pathological findings in 62 autopsied patients with peptic ulcer, both on gross (spangled) and on microscopic examination (stippled).

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Submitted May 15, 1951.

either as the primary disease or as a concomitant finding. We were interested to ascertain not only the changes present in the liver, but also to determine whether such liver changes are caused by the peptic ulcer, per se or are simply a co-incidental finding.

MATERIAL STUDIED

In the period from 1931 to 1950, 62 autopsies were encountered at Beth Israel Hospital, New York, with the pathological diagnosis of peptic ulcer (gastric or duodenal). The condition was often found in connection with other diseases such as malignancy, leukemia, arteriosclerosis, cirrhosis, chronic passive congestion, etc. Some have been cases of post-operative gastric surgery, for bleeding, perforating, or penetrating ulcers. Sex and age were noted, as well as the clinical diagnosis, the general anatomical diagnosis, the microscopic liver findings, and the pathological findings in the stomach or duodenum as to type and location of the ulcers.

Sex: 47 males and 15 females were noted, making a ratio of 3:1. This is similar to the ratio reported by us in a clinical study (9) of 439 duodenal and 48 gastric ulcer patients.

Age: The age groups ranged from 30 to 82 years, the majority being found from 50 to 69. Twenty-one per cent were encountered in the age groups from 50 to 59; 40% from 60 to 69. The average age for the entire group was 59 years. In military service the average age was 28 years; in private practice it was 30 to 50 years (9, 10).

Location of Ulcer: 22 of the 62 autopsy cases of ulcer were located in the stomach (35%), of which 14 were along the lesser curvature, 7 near the cardiac region and only one on the greater curvature. The age varied from 33 to 88, with an average of 63 years. This large number of non-malignant gastric ulcers in patients of such advanced age is of unusual interest, since many consider gastric ulcers as subject to early degeneration into malignancy, and therefore suitable only to surgical treatment. It makes us wonder if gastric ulcers in the aged cannot safely be observed more conservatively, rather than be subjected to immediate surgery.

Duodenal ulcers were found in 40 instances, making up 65% of the cases. The ratio of duodenal to gastric ulcers encountered in these autopsies is 2:1. This corresponds to that found by Schnitker and Haas (4). The usual accepted figure is 6 duodenal to one gastric ulcer. The ratio seems to vary considerably with the source of the statistical data. In a previous clinical study (9) we found the ratio to be 11:1. A survey reported in one of the army hospitals showed a ratio of 18:1 in the out-patient department as contrasted to 9:1 in the hospital (11).

Of the 22 gastric ulcers 18 (82%) were uncomplicated, while only 4 (18%) were complicated. In contrast, 18 of the duodenal ulcers (45%) were uncomplicated and 22 (55%) were complicated. This shows that complicated ulcers are three times more frequent for the duodenal than the gastric type.

PATHOLOGICAL FINDINGS IN THE LIVER

A. *Fatty Liver Changes.*

Table I shows the pathological findings in the 62 patients studied, correlated with co-existing clinical conditions. It is of interest to note how often the gross appearance of the liver is reported as normal or insignificant while the microscopic findings indicate liver involvement (See Fig. 1). In 25 cases (40%) the diagnosis of no significant gross pathology of the liver was made. In this group of 25 cases 20 showed fatty infiltration on microscopic examination. In only 5 cases (8%) both microscopic and gross liver findings were negative. A typical case of severe fatty changes in the liver microscopically is shown in Fig. 2. The question that arises here is whether this high percentage of minimal liver changes in these patients of rather advanced age is due to the peptic ulcer or simply represents the natural pathology of advanced age.

The age groups of the patients showing fatty livers corresponds to the average age grouping of the total number of cases (See Table II). 36% occurred in the 60-69 year age group and 24% in the 50-59 year group. This close correspondence of pathology to the age grouping indicates that the presence of ulcer was not the sole factor in producing the liver changes. Other complicating factors were present

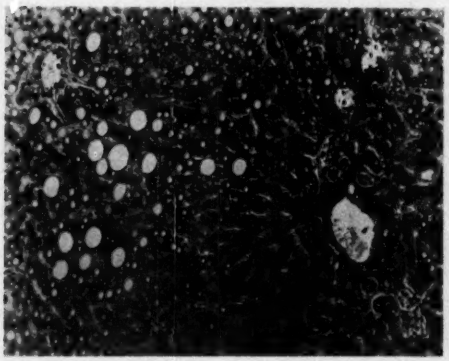

Fig. 2: Autopsy #48. A. H., Male, 66, showing typical severe fatty changes in the liver.

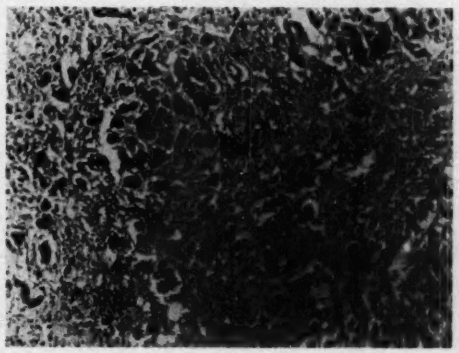

Fig. 3: Autopsy #53. L. S., Male, 44, showing typical picture of Laennec's cirrhosis.

TABLE 1

FINDINGS IN 62 PATIENTS WITH PEPTIC ULCER AUTOPSIES 1931-1950

			Type of Ulcer						Co-Existing Conditions										Pathological Findings in the Liver
#	Age	Sex	Duodenal	Gastric	Post-Operative	Bleeding	Penetrating	Perforating	Pulmonary	Vascular	Arteriosclerosis	Hypertension	Coronary	Obesity	Diabetes	Gall Bladder	Adhesions	Cancer	Nephritis	
			A_1 Cases Showing Fatty Changes in Liver Both Grossly and Microscopically																	
1	33	F		x												x				Fatty Infiltration
2	68	M	x															x		Fatty Infiltration
3	50	M	x					x									x			Fatty Changes
4	73	F	x											x		x				Severe Fatty Changes
5	55	M		x							x	x							x	Fatty Infiltration
6	52	M	x					x		x				x			x			Severe Fatty Changes
7	56	M		x					x				x							Severe Fatty Changes
8	65	M	x									x		x						Severe Fatty Changes
9	38	M	x				x			x										Severe Fatty Changes
10	45	F		x			x		x											Slight Fatty Changes
11	65	M	x					x				x								Fatty Infiltration
12	63	F	x								x		x	x		x				Fatty Infiltration
13	66	M		x										x	x					Severe Fatty Changes
			A_2 Cases Showing Fatty Changes in Liver Microscopically (No Significant Gross Pathology)																	
14	44	M	x		x	x						x	x							Peripheral Infiltration
15	70	M		x							x									Fatty Vacuolization
16	60	F	x													x	x		x	Peripheral Fatty Infiltration
17	66	F	x							x	x			x						Central Fatty Changes
18	54	M	x		x			x	x											Fatty Changes
19	62	M	x		x					x										Central Atrophy with fat droplets
20	77	M	x						x				x							Slight Fatty Changes
21	50	M		x											x					Fatty Vacuoles
22	53	M	x			x										x				Fatty Infiltration
23	73	M	x					x							x	x				Moderate Fatty Changes
24	45	M	x							x										Moderate Fatty Changes
25	65	F	x				x										x			Fatty Infiltration
26	65	F		x						x	x									Moderate Fatty Changes with Infiltration
27	54	M		x														x		Slight Fatty Changes
28	64	M	x				x										x	x		Slight Fatty Changes
29	70	M		x			x													Slight Fatty Changes
30	34	F	x															x		Severe Fatty Changes
31	63	M	x			x														Slight Fatty Changes
32	43	M	x		x	x		x												Mild Fatty Changes
33	71	M	x				x										x	x		Some Central Fatty Changes
		Totals	23	10	4	4	6	6	4	6	5	4	4	6	3	6	6	5	2	

B CASES SHOWING CIRRHOSIS OF THE LIVER																	
34	65	M	x	x				x		x							Nutmeg Liver (Laennec's Cirrhosis)
35	69	F		x						x			x	x			Cirrhosis—moderate fatty changes
36	80	M	x							x							Nutmeg Liver
37	65	M	x				x			x							Cirrhosis
38	57	F	x					x		x		x	x	x			Early Portal Cirrhosis
39	60	M	x										x		x		Cirrhosis—Slight Fatty Changes
40	68	M	x			x				x							Portal Cirrhosis
41	60	M	x									x				x	Cirrhosis (Nodular)
42	54	M		x	x						x						Laennec's Cirrhosis
		Totals	7	3	1	1	1	2		6	2	1	3	2	2		
C CASES WITH MISCELLANEOUS CO-EXISTING PATHOLOGICAL CONDITIONS																	
1. CANCER																	
43	55	M	x														Stenosing Ca of Bronchus—Liver Shredded with Metastases
44	51	M		x													Mixed Cell Tumor of Parotid with Liver Metastases
45	51	M		x											x		Ca of Gall Bladder with Liver Metastases
46	69	M		x											x		Ca of Sigmoid with Liver Metastases
2. STASIS																	
47	37	M	x	x				x		x	x				x		Liver firm, hyperemic; stasis
48	68	M		x			x										Liver soft, hyperemic; stasis
49	65	M	x			x				x							Soft, hyperemic liver; stasis
50	76	M	x				x			x		x					Liver firm—Central stasis
3. LEUKEMIA																	
51	43	M	x		x												Very large liver, filled with leukemic infiltration
52	72	M	x							x							Myeloblastic Leukemia, Infiltration in Liver
53	60	F	x										x				Lymphocytic Leukemia, Infiltrations in Liver
4. RED INFARCT																	
54	77	F	x												x		Cyst of Liver with red infaret
55	43	M		x	x												Hemangiomata—Red Infaret of Liver
5. ABSCESS AND CYST																	
56	44	M	x				x	x									Multiple Liver Abscesses
57	60	F		x									x				Multiple Cysts of Liver Surface
D CASES WITH COMPLETELY NORMAL LIVERS (Gross and microscopic)																	
58	88	M	x						x	x							Normal Liver
59	39	M	x								x				x		Normal Liver
60	67	M	x	x	x						x					x	Normal Liver
61	35	F	x		x												Pale but normal liver
62	60	M		x	x		x										Pigmented, Normal liver

such as bleeding, coronary artery disease, hypertension, cholelithiasis, adhesions, obesity and diabetes (Table I). These conditions must play the dominant role in effecting the pathological liver changes.

TABLE II

Age Group	Entire Series # of cases	Entire Series percentage	Group with Fatty Liver Changes # of cases	Group with Fatty Liver Changes percentage
30-39	6	10	3	9
40-49	7	11	4	13
50-59	13	21	8	24
60-69	25	40	12	36
70-79	9	15	6	18
80-89	2	3	0	0
	62	100	33	100

CIRRHOSIS OF LIVER

Only 9 cases of the 62 showed cirrhosis of the liver (See Fig. 3 for typical microscopic picture of Laennec's Cirrhosis). Six of the nine showed general arteriosclerosis; 3 gallstones; and only 2 cancer. There is no doubt that such medical conditions can produce secondary liver changes. The average age here was 64 years and surely played an important role in accounting for the cirrhosis. Considering the importance of the concomitant diseases found associated with the ulcers we must regard the peptic ulcer as playing only a secondary role in producing the liver damage.

The remaining liver diagnosis of stasis, cancer, leukemia, abscess and infarct are coincidental liver findings and have no bearing on the present problems.

In the 62 autopsies of peptic ulcer reviewed, it is felt that the liver changes encountered (fatty infiltration or cirrhosis) were not due to the peptic ulcer per se. The age group was far advanced. The concomitant medical condition of senility, obesity, gallstones, diabetes, general arteriosclerosis and coronary thrombosis were sufficient in themselves to produce such liver changes.

SUMMARY AND CONCLUSIONS

62 autopsies of peptic ulcers encountered from 1931-1950 were studied. A ratio of 3 males to one female was present. The average age group was 69 years. 40% of the peptic ulcers fell in the age group from 60-69.

Twenty-two gastric ulcers (35%) and 40 duodenal ulcers (65%) were found. The ratio of 2 duodenal to one gastric ulcer is less than usually encountered clinically (11:1).

The liver showed no significant gross pathology in 25 cases (40%), but in only 5 of these cases (8%) was the microscopic completely negative. Microscopically fatty liver changes were found in 33 (53%), while cirrhosis in only 5 (15%).

The liver changes found in these peptic ulcer patients were part of a far advanced age, and were secondary to other medical conditions, such as adhesions, arteriosclerosis, cholecystitis, cholelithiasis, obesity, etc.

Studies of cholesterol, liver function tests and pathology findings at autopsy show no liver changes caused by chronic peptic ulcer, particularly the non-complicated type.

There is no conclusive evidence that hepatitis or liver changes such as cirrhosis may be caused by peptic ulcer.

There is no need at present to determine liver function nor utilize precautionary measures to prevent chronic hepatic changes in non-complicated peptic ulcer patients.

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GASTRIC ULCER: DIAGNOSTIC STUDIES IN 100 CASES

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INTRODUCTION

THE DIFFERENTIATION of the benign from the malignant gastric ulcer continues to present a difficult clinical problem. The history of the patient, as well as the laboratory, roentgenologic and gastroscopic findings have been used to aid in this differentiation. It is the purpose of this paper to record the results of such studies in a group of patients with gastric ulcer and attempt to evaluate their usefulness in this respect.

MATERIAL

A series of cases of gastric ulcer was assembled from the files of the Dayton Veterans Administration general hospital. All cases were included which met the following criteria: the presence of a gastric ulcer satisfactorily established by roentgenologic study, gastroscopic examination or direct specimen examination of surgical or autopsy material, and in addition, a sufficiently thorough clinical and laboratory evaluation to be useful in this study.

Of the one hundred cases thus selected, 86 were considered benign and 14 malignant. Forty-nine of the 86 benign ulcers were proved by tissue examination; the remaining 37 cases proved benign by their clinical course. Twelve of the 14 malignant ulcers were proved by microscopic examination; the two remaining cases were judged malignant by their subsequent course.

RESULTS

HISTORY:

Age: The age of the patient was of little value as an aid in the differentiation of benign from malignant ulcer of the stomach. The ages of the patients in this series are listed in Table I. The age indicated in this table represents the age at the time of hospitalization, at which time the diagnosis of gastric ulcer was established. In most cases this coincides with the age at which the patient was experiencing the most distress from his gastric ulcer. As can be judged from Table II, the ages listed in Table I do not indicate the age of onset of upper gastrointestinal symptoms.* It was felt that the use of the latter criteria would be misleading, since many patients had upper gastrointestinal symptoms and complaints for many years prior to the demonstration of a gastric ulcer. This is further substantiated by the results in the eighth paragraph below: a sizable number of patients had symptoms leading to previous upper gastrointestinal barium studies which revealed roentgenologic evidence of duodenal ulcer or a normal upper gastrointestinal tract. The ages as recorded here, then, represent the age at which the gastric ulcer induced symptoms of sufficient severity to require hospitalization and allow adequate diagnostic procedures to establish the diagnosis of gastric ulcer.

TABLE I

AGE IN BENIGN AND MALIGNANT GASTRIC ULCER

100 Cases

Age in Years	*Benign*		*Malignant*	
	No. of cases	Percent	No. of cases	Percent
0 to 9	0	0	0	0
10 to 19	0	0	0	0
20 to 29	7	8	1	6
30 to 39	7	8	3	22
40 to 49	7	8	0	0
50 to 59	42	49	3	22
60 to 69	22	26	7	50
70 to 79	1	1	0	0
80 to 89	0	0	0	0
90 to 109	0	0	0	0
Total	86	100	14	100

It can be seen from Table I that approximately three quarters of both the benign and malignant ulcers occurred in the sixth and seventh decades. Of the eight gastric ulcers occurring under the age of 30 years only one was malignant.

Ulcer Pain: Ulcer pain as used here indicates a history of post-cibal burning or gnawing mid-epigastric pain, which may also occur in the early morning hours, and is relieved by the ingestion of food or some form of alkali.

In this series 62 (72%) of the 86 cases of benign gastric ulcer gave a history of ulcer pain. Of the 14 malignant ulcers, nine (64%) experienced ulcer pain. Smith and Jordan reported that 64.5% of 541 benign gastric ulcers complained of epigastric postcibal pain, as did 69.4% of 59 malignant gastric ulcers (1). Ulcer pain was valueless in the differential diagnosis.

Duration of Upper Gastrointestinal Symptoms: The duration of symptoms is divided arbitrarily into various periods and the results are listed in Table II. All upper gastrointestinal symptoms were included in evaluating the duration. It is interesting to note that 42% of those patients with malignant gastric ulcer complained of upper gastrointestinal distress for more

TABLE II

DURATION OF UPPER GASTROINTESTINAL SYMPTOMS IN BENIGN AND MALIGNANT GASTRIC ULCER: 98 CASES

Years	*85 Benign*		*13 Malignant*	
	No. of cases	Percent	No. of cases	Percent
0 to ½	26	30	2	15
½ to 2	14	16	5	35
2 to 5	16	19	3	25
More than 5	29	35	3	25
Total	85	100	13	100

From the Veterans Administration Hospital, Dayton, Ohio.

This work was done under the supervision of the Dean's Committee of the University of Cincinnati College of Medicine, Cincinnati, Ohio. Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or the policy of the Veterans Administration.

*"Upper gastrointestinal symptoms" refers to anorexia, belching, bloating, feeling of fullness in epigastrium, nausea, cramping, epigastric pain, vomiting or/and true ulcer pain.

Submitted May 31, 1951

TABLE III

ANEMIA IN BENIGN AND MALIGNANT GASTRIC ULCER: 98 CASES

Hemoglobin	*Benign*		*Malignant*	
	No. of cases	Percent	No. of cases	Percent
Hgb. less than 10 grams (Anemia)	20	24	3	21
Hgb. 10 grams or more	64	76	11	79
Total	84	100	14	100

than two years. One of these cases of malignant ulcer gave a history of upper gastrointestinal symptoms for more than fifteen years. A history of upper gastrointestinal symptoms for more than two years in no way indicated that the patient had a benign lesion in the stomach.

Weight Loss: The patient with a benign gastric ulcer was as likely to lose a significant amount of weight as was the patient with a malignant ulcer. Sixty-four of the 86 cases of benign gastric ulcer gave an accurate history of weight loss; of these, 25% had lost more than 25 pounds. Nine of the 14 cases of malignant gastric ulcer gave an accurate history of weight loss; of these 22% lost more than 25 pounds. This finding was similarly recorded in the large series compiled by Smith and Jordan.

History of Gastrointestinal Bleeding: Of the 86 cases of benign gastric ulcer, 41% gave a history of one or more episodes of hematemesis and 34% of one or more tarry stools. Of the 14 patients with malignant ulcer, 36% had experienced hematemesis and 21% noticeable melena.

There was no significant difference in the incidence of gastrointestinal bleeding in benign and malignant gastric ulcer. This is further substantiated by the incidence of anemia and of guaiac positive stools in the two groups as seen in Tables III and IV. Approximately one quarter of the gastric ulcers bleed significantly regardless of their etiology.

Previous Roentgenographic Studies of the Upper Gastrointestinal Tract: Eleven (13%) of the 86 patients with a benign gastric ulcer had a previous x-ray diagnosis of duodenal ulcer; fifteen (17%) had had a previously reported normal upper gastrointestinal radiographic study. Four (29%) of the 14 patients with malignant gastric ulcer had a previous x-ray diagnosis of duodenal ulcer and three (22%) had a previously reported normal upper gastrointestinal tract on radiographic study. The history of a duodenal ulcer did not exclude the possibility of a malignant ulcer in the stomach.

LABORATORY:

Histamine Gastric Analysis: The results of analysis of fasting gastric contents for free hydrochloric acid following subcutaneous histamine injection are presented in Table V. Achlorhydria did not exclude a benign ulcer in the stomach, nor did a normal or elevated hydrochloric acid level exclude the presence of a malignant lesion.

TABLE IV

GUAIAC TEST ON STOOL IN BENIGN AND MALIGNANT GASTRIC ULCER: 63 CASES

Guaiac Positive Stool	*Benign*		*Malignant*	
	No. of cases	Percent	No. of cases	Percent
Positive	13	25	3	27
Negative	39	75	8	73
Total	52	100	11	100

TABLE V

FREE HYDROCHLORIC ACID ON HISTAMINE GASTRIC ANALYSIS IN BENIGN AND MALIGNANT GASTRIC ULCER: 77 CASES

Degrees of free HCL	*Benign*		*Malignant*	
	No. of cases	Percent	No. of cases	Percent
Achlorydia 0°	7	12	3	30
Hypochlorhydria 1-25°	10	14	2	20
Normal 26-75°	35	52	4	40
Hyperchlorhydria—more than 76°	15	22	1	10
Total	67	100	10	100

Anemia and Guaiac Positive Stools: These findings have been listed in Tables III and IV, and referred to above.

ROENTGENOLOGIC EXAMINATION OF THE UPPER GASTROINTESTINAL TRACT WITH BARIUM:

Size of the Gastric Ulcer on the X-Ray Film: The size of the gastric ulcer was accurately recorded in 41 cases. Seven (20%) of 35 benign ulcers were three centimeters or more in diameter. Two (33%) of the six malignant ulcers were three centimeters or more in diameter. The other 32 ulcers (78%) were less than two centimeters in diameter. The presence of a large gastric ulcer did not aid in the diagnosis of malignancy.

Associated Duodenal Ulcer or Duodenal Scarring: In 69 cases the duodenum was adequately visualized. Nineteen (33%) of 58 benign gastric ulcers and two (19%) of 11 malignant gastric ulcers were associated with significant changes in the duodenum. Smith and Jordan reported associated deformity of the duodenum on x-ray in 29% of 541 benign gastric ulcers and in 30.5% of 59 malignant lesions. Duodenal ulcer (in the past or the present) was not a reliable indication that the associated gastric ulcer was benign.

Location of the Gastric Ulcer by X-Ray: From Table VI it can be seen that over one-half of the malignant ulcers, as well as the benign, occurred in the body of the stomach on or nearest the lesser curvature. This is also well substantiated in the series of Smith and Jordan, who report 63% of 211 benign gastric ulcers and 57% of 47 malignant ones in this same region. Lesser curvature ulceration, or ulceration near the lesser curvature, then, offered no assurance of benignity.

Reliability of the X-Ray Appearance of Gastric Ulcer: The correct etiology of a gastric ulcer may not be

TABLE VI

LOCATION OF ULCER BY X-RAY IN BENIGN AND MALIGNANT GASTRIC ULCER: 62 CASES

Location	*Benign*		*Malignant*	
	No. of cases	Percent	No. of cases	Percent
Prepyloric	13	23	1	14
Body, on or nearest lesser curvature	39	71	4	58
Body, on or nearest greater curvature	0	0	2	28
In fundus	3	6	0	0
Total	55	100	7	100

reflected in its roentgenographic appearance. In 43 (52%) of the 82 cases studied by an upper gastrointestinal x-ray, the findings were thought to be sufficiently characteristic to permit an opinion regarding the etiology of the ulcer. Seventeen (50%) of the 34 benign ulcers were thought to be malignant by their x-ray appearance. Three (33%) of the nine malignant ulcers were thought to be benign.

GASTROSCOPY:

The appearance of the lesion may not be characteristic at gastroscopy. Gastroscopy was performed in 37 cases. An ulcer could be visualized in 25 (68%) of these cases. No ulcer was visualized in eight (28%) of 29 benign lesions and in four (50%) of eight malignant lesions. Of the 21 benign ulcers visualized, five (23%) were thought to be malignant by their appearance through the gastroscope. Of the four malignant ulcers seen, one (25%) appeared benign gastroscopically.

SUMMARY AND CONCLUSIONS

The differentiation of a benign from a malignant gastric ulcer did not seem to be materially aided by the usual evidence derived from the patient's history, laboratory findings, x-ray studies and gastroscopic examination. In the 100 cases of gastric ulcer reviewed above, no single determination or group of determinations proved to be reliable in separating the benign from the malignant lesion. Furthermore, the findings in any one given case of gastric ulcer were often entirely misleading in this regard. It would seem, then, that the problem in management presented by the patient with a gastric ulcer may best be met by other means—i.e. either by immediate surgical resection (2) or, more conservatively, by a closely supervised trial of strict medical treatment with repeated studies (1) and thence surgical intervention only in those patients who respond poorly or who develop a recurrence of the lesion.

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GALLBLADDER DISEASE IN MEN: NEED FOR EARLIER DIAGNOSIS AND TREATMENT

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INTRODUCTION

THE RELATIVELY frequent occurrence of gallbladder disease in the female, and the "fair, fat, forty, fecund, flatulent female," legend which has been stressed in textbooks, literature, and teaching clinics, has led many to believe that gallbladder disease is a rare curiosity in men. From observations in a large charity hospital, (Cook County Hospital) and in private practice, we were impressed with the fact that gallbladder disease in men occurred frequently, but that it was not commonly considered and diagnosed in the early stages before the appearance of complications. At the Cook County Hospital, it was found that many men, ill with gallbladder disease, were often misdiagnosed as various functional or organic gastro-intestinal entities, before more definite symptoms of biliary tract involvement, such as colic or jaundice appeared. Also, while studying jaundiced patients, it was found that calculous jaundice was fairly prevalent among men. In private practice, too, we met a number of men who were ill with gallbladder disease, and who were previously studied for various gastro-intestinal disturbances, but considered normal mainly because the biliary tract was not investigated.

The relatively common occurrence of gallbladder disease in men in a clinical survey, led us to study this problem also in post-mortem material. Records of nine thousand and eighty-four autopsies performed over a period of ten years at the Cook County Hospital were examined. In one thousand and thirty-five of these, evidence of gallbladder disease was found. The latter records were analyzed according to sex, age groups, race and complications.

TABLE I

PERCENTAGE OF GALLBLADDER DISEASE, ACCORDING TO SEX, FOUND AMONG 9084 POST-MORTEM EXAMINATIONS—COOK COUNTY HOSPITAL

	Post-Mortems		Gall Bladder Disease	
	Number	Percent	Number	Percent
Male	5583	61	450	8
Female	3501	39	585	17
Total	9084	100	1035	11

From the Department of Internal Medicine and the Gastro-Intestinal Clinic of Cook County Hospital and the Department of Internal Medicine, University of Illinois, College of Medicine, Chicago, Illinois.

Submitted June 1, 1591.

RESULTS

Sex—Gallbladder disease was approximately twice as common in women (17%) as in men (8%), with 11 per cent of the patients coming to post-mortem revealing evidence of this condition (Table I). This result

TABLE II

NUMBER OF CASES AND PERCENTAGE DISTRIBUTION BY AGE GROUPS OF 1035 GALLBLADDER DISEASE CASES FOUND AT AUTOPSY

Age Group	Total Number	Men		Women	
		Number	Percent	Number	Percent
-39	77	26	6	51	9
40-59	383	157	34	226	39
60+	575	267	60	308	52
Total	1035	450	100	585	100

agrees with the experiences of other investigators (1, 2, 3).

Age—The highest percentage of gallbladder disease in both men (94%) and women (91%) occurred in the age groups of 40 and over (Table II). In men, 6 per cent of the cases occurred in the age groups below 39; 34 per cent came in the age group of 40-59; and 60 per cent in the age group of 60 plus. In women, 9 per cent of the cases occurred in the age groups below 39; 39 per cent in the group 40-59; and 52 per cent in the group of 60 and over. These findings also agree with those of previous publications (4, 5).

Race—One hundred and ninety-eight (19%) of the above ten hundred and thirty-five cases were colored and eight hundred and thirty-seven (81%) were white. Since about half of the autopsy material consisted of colored patients, the low percentage of gallbladder disease among the colored group is noteworthy and confirming of observations reported in the literature (6).

Complications—In two hundred and fifteen of the ten hundred and thirty-five cases complications were found.

Thirteen types of complications in one or more combinations were found in the following order of frequency (Table III); calculous jaundice (115), dilated intra and extra hepatic ducts (45), ascending suppurative cholangitis (31), splenomegaly (20), obstructive biliary cirrhosis (20), sub-phrenic abscess (16), post-operative peritonitis (16), cholecysto-duodenal fistula (11), liver abscess (8), hydrops of the gallbladder (8), perforation of the gallbladder (5), empyema of gallbladder (5), and cholecysto-(transverse) colic fistula (1).

Ninety-seven or 22% occurred among 450 men and one hundred and eighteen or 20% occurred among women (Table IV).

Most of the complications in both male and female were found in the age group of above 40 (99% and 92%, respectively). The percentage of complications increased with advancing age, both in the male (1% in the under 39 year age group, 37% in the 40-59 and 60% in the 60-and-over age group), and in the female (8% in the below 39 age group, 39% in the 40-59 and 53% in the 60-and-over age group). (Table V).

TABLE III

TYPE AND NUMBER OF COMPLICATIONS* FOUND AMONG 215 CASES OF GALLBLADDER DISEASE WITH COMPLICATIONS, AUTOPSIED AT COOK COUNTY HOSPITAL

Type of Complication	Number of Complications
Calculous Jaundice	115
Dilated Intra and Extra Hepatic Ducts	45
Ascending Cholangitis	31
Splenomegaly	20
Obstructive Biliary Cirrhosis	20
Sub-phrenic abscess	16
Post-Operative Peritonitis	16
Cholecysto-Duodenal Fistula	11
Liver Abscess	8
Hydrops of Gallbladder	8
Perforation of Gallbladder	5
Empyema and Gallbladder	5
Gallbladder—Transverse Colon Fistula	1

*One or more complications may be present in one patient.

Jaundice which is usually considered one of the significant complications of gallbladder disease occurred in 115 cases. It occurred as frequently among males (11%) as among females (11%) (Table VI). The majority of cases with jaundice both in males (96%) and females (89%) occurred in the 60-and-over age group (Table VII). The percentage of cases of jaundice increased steadily with increasing age groups. Thus, in the males, none occurred below the age of 39, 44% in the 40-59, and 56% in the above 60 age group. In the females,12 per cent occurred in the 39-and-under age group, 31 per cent in the 40-59, and 57 per cent in the 60-and-over age group.

DISCUSSION

Gallbladder disease in men not recognized—Many clinicians, even today, forget that a man complaining of indigestion can have gallbladder disease. Because of this, the presence of cholecystitis and/or cholelithiasis in males is still considered by some to be a rare curiosity, and so these diseases often are either not diagnosed or misdiagnosed as some other gastro-intestinal disturbance. Thus, of 45 patients with perforated gallbladder previously reported by us (7), the diagnosis of billiary tract disease was made in 32 per cent of the women and only 12 per cent of the men. Moreover, a review of the charts of all patients discharged from the Cook County Hospital with the diagnosis of gallbladder disease (with and without stones) during a period of one year, revealed that on admission, gallbladder disease was correctly diagnosed in 80 per cent of the women and in only 43 per cent of the men. While the percentage of occurrence of gallbladder disease on autopsy material among men is only half that of women, it surely cannot be considered a rare condition. When it occurs it creates a sizable mortality among men, especially in those over age 40.

Complications—The disease is as serious and severe among men as women, for the percentage of all complications which are responsible for deaths among men (22%) with gallbladder disease is as high as among women (20%). Calculous jaundice, the most common complication, was found as frequently among men (11%) as among women (11%).

Others, too, have shown that the percentage of complications among men having gallbladder disease is as high or higher than that among women. Thus, Johnstone and Ostendorph (8) reporting on 22 cases of cholecystitis with perforation, found 22 or 68% to be in men, while 10 or 31% were in women. Cole (9) observed that whereas men were not as likely as women to have cholecystic disease, they were much more likely to have complications when it did develop. Diffenbaugh and MacArthur (10), in their series of mortality statistics from gallbladder disease, noted that,

TABLE IV

NUMBER OF CASES WITH COMPLICATIONS AND PERCENTAGE DISTRIBUTION BY SEX, AMONG 1035 GALLBLADDER DISEASE CASES FOUND AT POST-MORTEM

Sex	Number of Gallbladder Patients	Number of Patients with Complications	Per Cent Complications
Male	450	97	22
Female	585	118	20
Total	1035	215	21

although men comprised only 27.3 per cent of the total cases, they had 50 per cent of the deaths.

Reasons for and Results of Delayed Diagnosis—In our opinion delayed diagnosis of gallbladder disease in men, until after the appearance of complications, is due mainly to not thinking of this disease in the differential diagnosis of upper abdominal pain. When a male with vague upper abdominal symptoms seeks medical advice, he is usually studied for evidence of an upper gastro-intestinal lesion. Should an examination fail to reveal any pathology, he is considered a case of "nervous stomach," spastic colon, or some other form of functional bowel disturbance, and is treated empirically and symptomatically. The patient alternates between periods of good and poor health over a period of years and in many instances reaches a stage of semi-invalidism. Not until there are additional and more specific biliary tract symptoms, such as severe pain located in the upper right quadrant with characteristic radiation (colic), subicteric tinge, definite jaundice or a palpable mass in right upper quadrant, will the biliary tract be suspected. The length of time from the onset of the vague abdominal symptoms to the appearance of complication varies from months to years. In many men the correct diagnosis and surgical relief of the cholecystopathy is usually not made until late in the disease, and at an older age period, at which time, there may be complications which create mortality.

On the other hand, in a woman, vague upper abdominal distress usually evokes an immediate gallbladder investigation. Findings of calcified stones in any type of gallbladder or soft stones in a visualized gallbladder, usually leads to surgery. Thus, a greater percentage of women are operated in the early stages of the disease, and at a younger age period, thereby preventing complications and deaths.

That men undergo surgical relief at a later stage in the illness and therefore have a considerably higher mortality as compared with that of women, has been shown by Bachhuber (11). His statistics indicate that the greatest incidence for surgery upon the biliary tract was between age 30 and 39 in the female, and age 40 and 49 in the male.

Diffenbaugh and MacArthur, (10), in a study of age and sex groups at the time of operation, stated that the peak age at the time of operation in their series was age 40 to 50 for women and 50 to 60 for men.

Importance of early diagnosis and treatment—Once a diagnosis of gallbladder stones is made, surgery should be performed early, unless there are definite contra-indications. Progress in surgical technique has reduced operative mortality to as low as 0.5 per cent in uncomplicated gallbladder surgery. Delay in surgery, however, leads to higher mortality.

Graham, (12), illustrated the dangers of delayed surgery by citing operative mortality figures for cholecystectomy. Thus, if operation is performed after two attacks, the mortality is 2 to 3 per cent; after three or more attacks it is 8 to 9 per cent; in the presence of jaundice, 10 to 12 per cent; and in the presence of pancreatitis nearly 50 per cent. To delay operation, is, therefore, to invite trouble.

Galbladder disease is a recurrent and progressive disease and as the disease progresses, eventually, adjacent organs become involved in the pathologic process. Mortality increases commensurately with the number, extent and character of the resulting complications. One might mention only the increased surgical risk of common duct drainage and cholecystectomy as against a simple cholecystectomy. The risk is not only the immediately higher surgical mortality and morbidity due to common duct drainage, but also, the possibly later occurring changes in the common duct (Stricture). Moreover, when operation is delayed, the pathological changes which take place throughout the biliary tract system, are not only of local significance, but also impair the patient's general resistance. This necessitates more intensive pre-operative and post-operative treatment, requires more extensive surgery and multiplies the difficulties of the technical performance. Jaundice is a serious complication and obviously could be avoided by earlier diagnosis and surgical intervention. The jaundiced patient entails considerable pre-operative care, which is a considerable economic factor in prolonged hospital stay and cost of medication, and the patient also presents an added risk to the surgeon.

Others, (13, 14), too, believe that once indications for surgery are established, the earlier operation is performed, the better. With advancing age, surgical risk becomes more serious due to the fact that the patient may be suffering from some concomitant malady, such as degenerative diseases, arteriosclerosis, hypertension, coronary artery disease, diabetes and others. On the other hand, removal of a diseased gallbladder may relieve or lessen the severity of coronary disease, asthma, pylorospasm, and other reflex conditions.

TABLE V

NUMBER OF CASES AND PER CENT DISTRIBUTION BY AGE GROUPS AMONG 215 GALLBLADDER DISEASE PATIENTS WITH COMPLICATIONS, FOUND AT POST-MORTEM

Age Group	Total Number	Total Percent	Male Number	Male Percent	Female Number	Female Percent
-39	12	5	1	1	11	8
40-59	82	40	37	39	45	39
60+	121	55	59	60	62	53
Total	215	100	97	100	118	100

SUMMARY

1. Gallbladder disease constitutes an important problem among men, especially in the age group of 40 and over.

2. Gallbladder disease is as serious and severe a disease among men as among women.

TABLE VI

NUMBER AND PERCENTAGE OF CASES WITH JAUNDICE DISTRIBUTED ACCORDING TO SEX, AMONG 1035 GALLBLADDER DISEASE CASES FOUND AT POST-MORTEM

	Number of Gallbladder cases	Number of cases with Jaundice	Percent with Jaundice
Male	450	50	11
Female	585	65	11
Total	1035	115	11

TABLE VII

NUMBER OF CASES AND PERCENT DISTRIBUTION BY AGE GROUP AMONG 115 GALLBLADDER DISEASE CASES WITH JAUNDICE, FOUND AT POST-MORTEM

	Total		Male		Female	
Age Group	Number	Percent	Number	Percent	Number	Percent
-39	5	4	0	0	5	12
40-59	45	39	22	44	23	31
60+	65	57	28	56	37	57
Total	115	100	50	100	65	100

3. Gallbladder disease in men often is either not diagnosed or misdiagnosed as some other gastro-intestinal disturbance, mainly because it is not adequately considered in the differential diagnosis of abdominal symptoms.

4. Earlier recognition of gallbladder disease in men should result in earlier treatment with a subsequent reduction in complications and mortality.

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THE USE OF MULTIPLE INTESTINAL ADSORBENTS AS AN ADJUNCT IN THE MANAGEMENT OF NAUSEA AND VOMITING IN PREGNANCY

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NAUSEA AND vomiting occur in about fifty percent of women during the first three months of pregnancy. The distress produced is generally not serious, but is disturbing to the patient and the physician.

A majority of these patients respond to established measures of treatment. There are, however, some patients in whom these symptoms may be so severe as to become serious. This is particularly true when the patient loses her appetite because of the stomach's intolerance for liquids and foods.

The etiology of nausea and vomiting in pregnancy has not been definitely established. It has been suggested that substances formed in the body in disease may raise the excitability of the vomiting center to a level where afferent impulses, ordinarily of sub-threshold value, may become effective for the initiation of the reflex. It is of interest in this regard that substances formed in the body, e.g., adrenaline, choline and histamine, induce vomiting when applied directly to the center (1).

The concept that histamine may be an important etiological factor was proposed by Hofbauer (2). This concept was further investigated by Kappelar-Adler (3) in her studies of the histidine-histamine metabolism in normal and pathological pregnancies. She concluded from her results that this syndrome is probably a manifestation of histamine intoxication.

The symptoms, according to Finch (4), are due to an allergic action of the patient to the secretion of her own corpus luteum graviditatis.

Finch (5) pointed out that "one of the actions of histamine in producing allergic symptoms is to produce spasm of smooth muscle which is a part of nausea and vomiting complex."

Definite evidence of histaminase activity was found by Koloszynski (6) in sera of pregnant women and no such activity in non-pregnant women. He suggested that this enzyme may be an important link in the metabolism of histidine during pregnancy.

The Smiths (7) reported elevated levels of chorionic gonadotropin during this period, lending support to the thought that the syndrome should be classified as a true toxemia of pregnancy.

The work of Hansen (8), confirmed by Williams (9), shows that "the emptying time of the stomach during pregnancy is prolonged 50 to 130 minutes beyond the two hour period considered to be normal for non-

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Submitted May 21, 1951.

pregnant women." In a few gravid women, Hansen (8) found that the stomach never emptied itself entirely.

Vomiting of any kind may give rise to ketosis, if it becomes severe enough to produce carbohydrate starvation and lasts long enough to exhaust liver glycogen. Ketosis appears more rapidly and reaches greater intensity in pregnant than non-pregnant women.

It has been proposed by Kydd and Peters (10) that, in vomiting of pregnancy and in toxemias, ketosis occurs as a result of starvation. Vomiting in these conditions gives rise to acidosis, not alkalosis, because ketone bodies are produced in excess and at the same time there is a deficiency of free hydrochloric acid in the gastric secretions.

We postulated that other toxic substances in addition to histamine are formed in the gastro-intestinal tract as a result of hypochlorhydria with breakdown of food elements by bacteria. It was, therefore, presumed that a preparation having the capacity to adsorb such intestinal toxic substances should prove effective in the management of nausea and vomiting in pregnancy. It was deemed imperative that the preparation should not interfere with the absorption of essential food elements.

Resion,* consisting of polyamine anion exchange resin, synthetic sodium aluminum silicate and synthetic magnesium aluminum silicate, was reported (11) as having the required attributes for an ideal intestinal adsorbent. It was observed that this combination possessed the capacity to inhibit lysozyme (12), to remove toxic amines such as tyramine, histamine, putrescine and cadaverine (13), to adsorb bacterial metabolites (14) and to remove agents comparable to shellfish poison (15). Essential food factors, such as vitamins, minerals and amino acids were not removed.

Impressed by the reports on Resion, we decided to try this preparation clinically in the treatment of nausea and vomiting in pregnancy.

MATERIALS AND METHODS

A total of 327 patients registered in the obstetrics out-patient clinic between July 1, 1949 and July 1, 1950. No effort was made to subdivide these patients as to age, parity or social status.

As in most clinical cases in contradistinction from private cases, the majority of our patients had successfully combatted the episodes of nausea before registering. Most of the patients who reported within the first three months of pregnancy, did so because of uncontrolled nausea and vomiting.

An analysis of the total registration revealed the following: 1. There were 137 patients who reported before the fourth month of pregnancy. Eighty-six of these patients complained of nausea and vomiting which caused them discomfort and required treatment. Two of these patients were classified as hyperemesis gravidarum and required hospitalization. 2. There were 190 patients who registered after the third month of pregnancy. A history of some degree of nausea was obtained from 180 of these patients, but they were safely over this stage. There were ten patients who still complained of their symptoms and required treatment.

*Resion—Supplied by the Medical Research Department, The National Drug Company, Philadelphia 44, Pa.

The number of patients requiring treatment for nausea and vomiting was 96 out of a total registration of 327.

Our routine procedure in the management of this syndrome consists of frequent small dry feedings supplemented with multi-vitamins, iron and calcium when these can be tolerated. Whenever deemed necessary, psychotherapy is also used.

The 94 ambulatory patients were placed on our routine treatment and their progress followed in the out-patient clinic.

The two patients with hyperemesis gravidarum were hospitalized and treated by starvation, sedation and parenteral feedings. One patient was completely relieved by this regimen, the second patient was relieved but had to be rehospitalized because hyperemesis recurred. Following her second discharge from the hospital, she was placed on Resion, continued this medication for two months and reported no futher difficulties.

The routine treatment employed by us controlled the syndome satisfactorily in 66 of the 94 patients treated. Twenty-eight patients were not benefitted and were placed on other treatment.

Of the 28 patients not relieved by small dry feedings, 9 were given pyridoxine intravenously with good results in 3 and failure in 6 patients. Five patients were given dramamine with failure in all cases. Thus, out of this group, 14 patients did not respond to continued dietary measures, 6 failed on pyridoxine and 5 did not respond to dramamine. There were 25 patients not relieved by the various measures tried, and these were finally placed on Resion. One to two teaspoonfuls of Resion on rising, between meals and at bedtime, represented the dosage schedule. The patients continued with the regular routine prescribed for all outpatients.

Results with Resion as supplement: Eighteen patients out of 25 on routine therapy supplemented with Resion responded favorably. The 7 patients who failed to respond all gave a history of vomiting the entire period of gestation in previous pregnancies. It was felt that the psychic element so predominated the picture that no satisfactory results could have been expected by medical management.

Rapid excessive weight gain was a complication in 36 of the 66 patients adequately controlled by frequent small dry feedings. The 36 patients were divided into two groups:

Group I: Consisted of 25 patients placed on low caloric diets.

Group II: Consisted of 11 patients placed on low caloric diets plus Resion—two teaspoonfuls between meals and at bedtime.

RESULTS

Group I: Although the syndrome of nausea and vomiting was adequately controlled in the whole group, excess weight gain continued to be a problem in more than 50% of these patients.

Group II: All 11 patients on low calorie diets plus Resion as supplement were adequately controlled from the standpoint of excess weight gain as well as nausea and vomiting.

SUMMARY

The possible etiologic factors in nausea and vomiting in pregnancy are reviewed.

Resion, a multiple adsorbing agent, is described.

Out of a total registration of 327 patients in our pre-natal clinic, 96 required treatment for nausea and vomiting of pregnancy. Two of these patients required hospitalization.

Sixty-six patients were relieved by routine treatment as prescribed in the clinic.

Three patients were relieved by pyridoxine intravenously.

Twenty-five patients failed to be relieved by dietary measures, pyroxine or dramamine. Eighteen of these patients were relieved by routine treatment plus Resion as a supplement. A heavy psychic overlay may be the reason for failure in the seven patients not relieved.

Rapid excessive weight gain was a complication in thirty-six of the sixty-six patients relieved by routine measures. Twenty-five of these were placed on low calorie diets and eleven patients on low calorie diets plus Resion as supplement.

Excessive weight gain continued to be a problem in a little more than fifty percent of the low calorie diet treated patients; however, the syndrome of nausea and vomiting continued to be controlled.

Normal weight gains were maintained and nausea and vomiting relieved in all eleven patients on low calorie diets plus Resion as supplement.

COMMENT

Any problem which affects fifty percent of a physician's obstetrical practice must receive serious consideration.

We consider it sound medical procedure to treat nausea and vomiting of pregnancy while it is in a moderate form, thus preventing a possible aggravation of this syndrome and the onset of hyperemesis.

The plethora of medicaments used for the treatment of this syndrome adequately attests the lack of a specific therapy. Our studies seem to indicate that Resion, a multiple adsorbent combination, is an important addition to the physician's armamentarium for the treatment of nausea and vomiting of pregnancy.

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ABSTRACTS ON NUTRITION

McQUEEN, E. G.: *The syndrome of gout.* Med. J. Australia, May 5, 1951, 644-650.

The causes of gout may be many, hence the use of the expression, "the syndrome of gout." The one essential to the diagnosis is abnormal elevation of the blood uric acid. Most cases are hereditary, the determining gene being an autosomal dominant. Excessive blood uric acid may at times occur in blood diseases due to nuclear destruction. Uric acid retention may occur in advanced renal disease. Nephrosclerosis most frequently is found in gout, and may be intimately related to Seyle's diseases of adaptation. The acute gouty arthritis attack may be due to a depression of adrenal secretion, since the administration of ACTH and cortisone immediately relieves the attack.

PETERS, J. H.: *Vascular complications of diabetes.* Am. Pract. & Dig. Treat., 2, 8, Aug. 1951, 669-72.

Arteriosclerosis is seen with increasing frequency in aging groups with some hypertension or diabetes or who are overweight. Hardening of the arteries occurs eventually in virtually all diabetics in one or another of its forms. After a patient has had diabetes 20 years, it is 9 to 1 that he will have detectable sclerosis. The incidence of retinitis is higher than any other single sclerotic lesion. Cardiovascular disease kills from 30 to 60 percent of diabetics. Before long the handling of arteriosclerosis may become the principal aim of our therapeutic program. Retinal changes tend to occur earlier than hypertensive and nephritic changes. In the presence of serious vascular lesions, hypoglycemic reactions are particularly dangerous.

RODBARD, S., BOLENE, C. AND KATZ, L. N.: *Hypercholesteremia and atheromatosis in chicks on a restricted diet containing cholesterol.* Circulation, IV, 1, July 1951, 43-46.

The effect of a limited intake of a cholesterol-enriched diet on the tendency to hypercholesteremia and atherogenesis was studied in chicks. Limitation of dietary intake to two-thirds of that normally taken did not protect against the development of hypercholesteremia and atherosclerosis in these malnourished

birds. The tendency to atherosclerosis and hypercholesteremia is correlated with the cholesterol ingested per kg. of body weight. Atherosclerosis therefore occurs in starved animals and in the absence of obesity or over-eating.

ELLENBURG, L. L. AND PETERSON, J. C.: *Chronic galactosemia*, Am. Pract. and Dig. Treat., 2, 7, July 1951, 602-08.

The authors present a case of galactosemia and extended reference is made to the few cases on record. It is a rare disorder of metabolism in which there is a congenital defect of the liver, wherein the conversion of glactose into glycogen is impaired. Cutting out milk and galactose-containing foods appears to benefit these cases.

GARN, S. M., GERTLER, M. M., LEVINE, S. A. AND WHITE, P. D.: *Body weight versus weight standards in coronary artery disease and a healthy group.* Ann. Int. Med., 34, 6, June 1951, 1416-1419.

The authors compared, as to weight, 97 men who had experienced myocardial infarction prior to the age of 40, with 146 healthy men of comparable age, occupation and mode of living. Both groups were "overweight" in comparison with the norms at all age levels, and to the same degree. This study indicates that when truly comparable controls are used, those who early experience myocardial infarction are not more overweight or obese as a group than are the controls. Perhaps both groups were overweight. What, actually, is the norm?

MITRA, H. N.: *Observations on argemone oil and detoxicated argemone oil.* J. Indian Med. Assn., XX, 9, June 1951, 315-316.

Although the literature on the subject of epidemic dropsy is enormous, and many etiological theories have been advanced, Mitra now believes that the disease in India is caused by ingestion of impure mustard oil contaminated with Argemone oil. The latter contains two toxic alkaloids, sanguinarine and dihydrosanguinarine. A process has been found for removing these two alkaloids from Argemone oil. The author reports some animal experiments which appear to demonstrate the toxic character of Argemone oil and its capacity for causing edema and changes in the kidney and suprarenal glands particularly.

SPRAY, G. H., FOURMAN, P. AND WITTS, L. J.: *The excretion of small doses of folic acid.* Brit. Med. J., July 28, 1951, 202-205.

The authors studied the utilization of folic acid by measuring the excretion of small doses injected intravenously in four groups of subjects,—10 normal, 3 patients with steatorrhea, 5 patients with untreated pernicious anemia and 13 patients with pernicious anemia under treatment. The patients never excreted more of an injected dose than the normal subjects but the following excreted less,—3 patients with steatorrhea, 3 with untreated pernicious anemia and 2 of the p. a. patients under treatment. These results suggest that there may be a rapid and increasing utilization of folic acid in some instances of megaloblastic anemia. This implies a deficiency of folic acid, either real or conditioned, but the results do not determine which. Possibly both occur in different groups of cases.

RUDNIKOFF, I.: *Insulin and the carotid sinus.* Ann. Int. Med., 34, 6, June 1951, 1382-94.

The author shows, in a group of 10 diabetics, that insulin increases the activity of the carotid sinus reflex. Apparently ventricular standstill may prove fatal in some cases where sinus stimulation is applied following insulin administration.

SCHNITKER, M. A., MATTMAN, P. E. AND BLISS, T. L.: *A clinical study of malnutrition in Japanese prisoners of war.* Ann. Int. Med., 35, 1, July 1951, 69-96.

The authors made a very detailed study of 24 starved prisoners of war. Twelve had massive edema and 12 had no edema. In the dry group they found a consistently lowered blood cholesterol which returned promptly to normal under dietary treatment. This was the only essential difference in the two groups. The edema was not due to beri-beri. The clinical picture was one of nutritional hypoproteinemia with a sprue-like syndrome manifested by marked alterations of serum proteins, with or without edema, with glossitis, diarrhea and marked wasting. The presence of edema in some and not in the others may have been due to differences in sodium intake prior to capture, or in sodium clearance.

FIRSTBROOK, J. B.: *The newer knowledge of atherosclerosis.* Brit. Med. J., July 21, 1951, 133-138.

Experimental arteriosclerosis is due to feeding cholesterol, but the development of the disease is influenced by the blood pressure, the presence of adiposity, and other unknown factors. While it cannot be proved that dietary cholesterol is involved in human atherosclerosis, probably cholesterol should be restricted in this disease, although such a diet presents difficulties. Where hypothyroidism is present it should cautiously be corrected. The induction of hypothyroidism for angina pectoris seems unwise because of the probability of accelerating the underlying arteriosclerotic process. Certainly adiposity should be avoided. A diet low in animal fat has a low cholesterol content.

ROBERTS, E.: *The treatment of obesity with an anorexigenic drug.* Ann. Int. Med., 34, 6, June 1951, 1324-1330.

Sixty-four obese patients who had not been able to lose weight during a six months' dietary trial were treated with Dexamyl (a combination of Dexedrine and amytal) for appetite control. Within 3 months, 59 of these patients reduced their weight considerably, bringing 14 of them to normal and 28 within 19 percent of normal weight. Ten diabetics included in the study all lost weight, and those on insulin were able to reduce the dosage, sometimes by more than 50 percent. The 7 hypertensives treated with Dexamyl lost an average of 25 lbs.: in all cases but one, in which there was no change, the blood pressure was reduced.

VAN ITALLIE, T. B.: *Caloric priorities in parenteral nutrition.* Nutrition Reviews, 9, 7, July 1951, 193-197.

Parenteral nutrition will succeed only if the caloric demands of the patient who is unable to eat can be met, either parenterally or from his own stores. When such body stores are lacking, as usually is the case in chronic wasting diseases, caloric needs cannot adequately be met by the parenteral preparations now available. The need for a more effective intravenous calorigenic material is urgent. Fat emulsions plainly offer the only practical solution to this problem. It is hoped that the technical difficulties now preventing widespread use of them soon will be overcome. A harmless stabilizer for fat emulsions is needed as well as a consistently pyrogen-free oil.

EDITORIAL

ANTABUSE

Antabuse (i.e.) tetra-ethyl-thiuram disulphide is a worthwhile drug in reducing the list of previously unsalvageable alcoholics by commonly accepted therapeutic procedures. Thus of the 40 per cent inebriates in that category one third are definitely improved and another third somewhat improved, while there remain the third failures.

A program is outlined as follows: If the patient is willing to cooperate or a member of the family assumes

the responsibility and the patient has no evidence of renal or hepatic damage and no advanced cardiovascular disease, the patient is given 1.5 G. the first day, 1 G. the second and .75 G. or .5 G. daily for maintenance. The fourth day he is given 40 cc. whiskey and his reaction observed. This is repeated on the fourteenth day with 20 cc. whiskey and at gradually lengthening intervals. This repeated testing tells the physician if the patient is following his instructions and serves as a reminder to the patient of what will happen if he starts to drink. The cumulative effect of the drug is pointed out to discourage any idea that a short respite off the drug will allow one to drink heavily.

The action of antabuse is to inhibit cellular respiration and it is a competitive hydrogen acceptor, thus ascorbic acid given intravenously in 1 G. dosage is antagonistic. Probably the cyanide radicals inactivate the tissue dehydrogenases. The level of blood acetaldehyde is increased several fold even though elimination does not appear to be interfered with, suggesting that an alternate more complete oxidation pathway has been blocked. It is well to realize that patients with diabetes mellitus are not candidates for antabuse therapy and that fast acting barbiturates may show marked potentiation in patients receiving antabuse.

Electrocardiograms taken before and after six months or more of therapy show minor changes in two thirds of the cases (i.e.) flattening of T wave in one or more leads. This would appear to be reversible in the majority of cases. However, a patient with a history of angina but negative electrocardiogram may be made worse by this therapy. In a group of unselected patients in the fourth and fifth decade of life with no previous history or clinical evidence of cardiac disease including electrocardiogram, another tracing taken at the height of the antabuse-alcohol reaction showed S T segment deviation in 20 per cent characteristic of coronary insufficiency and the clinical reaction was different with hypotension, constriction feeling at lower end of sternum, and tendency to nausea and vomiting. Even though myocardial anoxia could cause this change it must be conditioned by coronary flow.

Thus, it would appear important to evaluate every patient electrocardiographically in this way and to select only patients with no significant change for continuation of antabuse therapy. The antabuse-alcohol reaction could take its place with the Master and/or Levy tests in demonstrating latent coronary insufficiency or evaluating efficiency of coronary vaso-dilators.

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Wilson, W. W., and McCabe, E. S.: Unpublished observations.

BOOK REVIEWS

TEXTBOOK OF THE ROENTGENOLOGICAL DIFFERENTIAL DIAGNOSTIC. VOLUME 2: DISEASES OF THE ABDOMINAL ORGANS. LEHRBUCH DER ROENTGENOLOGISCHEN DIFFERENTIALDIAGNOSTIK. BAND 2: ERKRANKUNGEN DER BAUCHORGANE. Werner Teschendorf. 608 pages, 1081 illustrations. Georg Thieme, Stuttgart. (Grune & Stratton, New York City, agents) 1950. $17.30.

This is the second volume of a textbook on roentgenological diagnosis. It covers the abdominal organs and includes, besides the digestive tract, the urological tract. Teschendorf's book is a marvelous work of thoroughness. The examination of the gastrointestinal tract will be of especially great interest to the readers in the United States as there exist few publications which, using modern methods, cover this subject. There are extensive studies of the mucosa of stomach, duodenum, and intestines. Of course, the spotfilm technique is described and many informative illustrations are given. The most important part of the book are its 1081 roentgenograms, the reproduction of which is faultless. Just to mention some of the excellent features, is the chapter on the appearance of the stomach after operations. This chapter alone has over 100 illustrations. There are schematic drawings of the operative procedures. Very valuable are the illustrations of marginal ulcers and local recurrences of carcinomas. The chapter on pathology of the appendix is very informative. The section on small intestinal pathology is not as exhaustive as other parts of the book. There are chapters on studies of the urological system, pancreas, spleen and other abdominal tumors. The literature is very well covered. The references are given at the bottom of each page, containing many references to the American literature.

This textbook is written in German, its style is good and clear. Due to the innumerable illustrations, it will be of extreme value to all those interested in gastroenterology and roentgenology. Even if the reader is not entirely familiar with the German language, it is visually so clear that any physician can understand it and profit by its use.

Franz J. Lust.

MANAGEMENT OF CELIAC DISEASE. Haas and Haas, J. B. Lippincott Company, June 4, 1951.

"Management of Celiac Disease" by Sidney V. Haas and his son Merrill P. Haas, is a handy monograph containing a summary of our knowledge of the disease to date. It has a good bibliography of 668 references. Sidney Haas will be remembered for his valuable contributions in the use of atropin in pyloric stenosis and for the banana diet for celiacs. He has had extensive experience, the book reporting the results of 670 cases, 320 treated and followed up for several years. Practically all recovered completely within 18 months on a regime of protein milk, bananas, meat and cheese. Later, other fruit, eggs and some vegetables were added and vitamin supplements were recommended. The diet is strictly maintained for at least 12 months, and then cereals, potatoes and sugars are added one at a time. After three months, plain milk is added, and if the milk is tolerated the cure may be considered complete, according to the authors.

The disease is defined as a protracted intermittent diarrhea resulting from the ingestion of carbohydrates other than those in fruits, some vegetables and protein milk. The disease may occur any time after birth, but is most common between the ages of 6 and 12 months.

The authors offer a hypothesis for the etiology of this disease. It is that there is some mechanism in the intestinal tract of the celiac sufferers which converts polysaccharides into a substance like an anthro-quinone which irritates the intestinal tract. A high proportion of monosaccharides is characteristic of the diet which helps these patients, and the common factor producing diarrhea is a large proportion of polysaccharides. Either an enzyme or a germ causes this abnormal metabolism, according to the authors who tend to a microorganism theory rather than the enzyme.

This reviewer would like to have had more space devoted to the extensive work of Dr. Dorothy Anderson in celiac disease.

The book is a good reference volume for pediatrists and gastroenterologists who often are called upon to treat this disease syndrome.

Edward T. Wilkes, M. D.

ALLERGY IN RELATION TO PEDIATRICS. Bret Ratner, M. D., Bruce Publishing Co., St. Paul and Minneapolis, 1951, $3.75

Some 16 well-known authors contribute individual chapters to the somewhat intricate problems of allergy as it is ex-

perienced by children. In some ways the manifestations of, and the systemic reactions to, allergy are different in childhood from adulthood. We have therefore a new subspecialty—pediatric allergy—which obviously receives the sanction of The American College of Allergists, Inc., who sponsor the book.

A COLOR ATLAS OF MORPHOLOGICAL HEMATOLOGY. Geneva A. Daland, B. S., Edited by Thomas Hale Ham, M. D., University Press, Cambridge, Mass., 1951, $5.00.

This new and beautiful book contains detailed information on the blood findings in some 12 important diseases as well as general chapters on blood technique and descriptions of normal blood. It is profusely illustrated with large color plates of blood smears. It is decidedly helpful and should be read by every internist.

GOOD FOOD FOR BAD STOMACHS, Sara M. Jordan, M. D. and Sheila Hibben. Doubleday & Co., Inc., Garden City, New York, 1951, $2.95.

This is a cook-book for the use of victims of peptic ulcer. Dr. Sara M. Jordan feels that ulcer patients, while eating safely, ought also to be assisted in eating with pleasure. So, with the assistance of a renowned dietitian, Mrs. Sheila Hibbon, she has produced about 500 selected recipes with indications for their use in ulcer particularly. This is a valuable book to place in the hands of any dyspeptic. Congratulations to Dr. Jordan for a nice piece of work.

METABOLIC METHODS. C. Frank Consolazio, Robert E. Johnson, M. D. and Evelyn Marek, M. A., 471 pages, The C. V. Mosby Company, St. Louis, 1951, $6.75.

This work covers the technical and interpretative aspects of all metabolic tests used in clinical medicine. Intentionally omitted is any description of isotopic, ultracentrifuge and electrophoretic techniques for the reason that as yet they are not widely used routinely in metabolic balance studies. The student will find complete details for biochemical procedures and function tests. Every clinical laboratory should possess a copy of this book.

GENERAL ABSTRACTS

HURWITZ, S. AND MCALENNEY, P. F.: *Trichobezoar in children.* Am. J. Dis. Child., 81, 6, June 1951, 753-761.

The authors review the subject of hairballs in the stomach, giving some interesting historical features. They also present two cases in children with valuable x-ray pictures of the stomachs. The symptoms of trichobezoar include pain, vomiting, constipation alternating with diarrhea, foul breath, anemia, exhaustion and intolerance to solids. X-ray and gastroscopy are both good methods of diagnosis. Treatment is surgical and prognosis excellent with early diagnosis, the mortality being less than 4 percent. Death, when it occurs, is due to inanition, intestinal obstruction or perforation. Both cases presented had been in the habit of swallowing strands of hair and chewing the fuzz off blankets.

PETERS, G. A. AND HORTON, B. T.: *Headache; with special reference to the excessive use of ergotamine preparations and withdrawal effects.* Proc. Staff Meet., Mayo Clin., 26, 9, Apr. 25, 1951, 153-161.

Ergotamine preparations if used excessively for migraine, frequently produce, on their cessation, withdrawal headaches. To avoid these withdrawal effects, as well as to avoid toxic symptoms, the drug should be used sparingly. The authors emphasize the fact that dihydroergotamine (D. H. E. 45) is less toxic and less likely to get the patient into trouble than ergotamine tartrate.

MULVANY, B.: *Limitations of a pure psychogenesis.* Med. J. Australia, Apr. 7, 1951, 505-510.

Mulvany is scarcely ready to admit the absolute causal role of psychogenesis in mental diseases. He seems equally unprepared to accept many of the hypotheses of psychosomatic medicine as valid, particularly those which attribute a diseased condition to a mental state. Psychogenesis may play an important but entirely non-specific role. Many psychotic episodes are due to some basic disease process of a tangible character. In illustration he cites a psychosis lasting several hours in a person suffering from psychomotor epilepsy. In this case the psychosis must have been caused by the epilepsy. The "diffuse basic anxiety" produced by stress may have found any one of several outlets—asthma, peptic ulcer, etc., depending entirely on local factors. It is always permissible and salutary to admit that the cause of a given disease is unknown.

DIBLE, J. H.: *Degeneration, necrosis and fibrosis in the liver.* Brit. Med. J., Apr. 21, 1951, 833-841.

A new conception of the pathology of liver degeneration, involving fatty change and necrosis, and ultimately leading to fibrosis has been developed. The conception that fatty infiltration of the liver is a precursor of the common form of cryptogenic portal cirrhosis finds little or no support from such evidence as this study has produced. It follows that any classification of human cirrhosis on such an etiologic basis is untenable. The two chief events which lead to portal cirrhosis are a previous hepatitis and a cryptogenic process, sometimes due to diet but not preceded by fatty infiltration or extensive necrosis. Either process results in progressive destruction of liver cells, associated with attempts at their regeneration. This occurring within the framework of fibrous scar tissue produces the nodular appearance so characteristic of many cirrhotic livers.

LAFORET, E. G., GREENLEE, J. J. AND O'BRIEN, E. J. *Acute appendicitis with radiopaque appendiceal lithiasis.* Am. J. Roent. Rad. Ther. 65, 867. June 1951.

The contribution of the radiologist to the evaluation of the routine case of acute intra-abdominal pathology has often been overlooked, but may nevertheless be significant. A simple flat roentgenogram of the abdomen may frequently reveal data of diagnostic importance. Appendiceal fecaliths are rendered radiopaque by an inflammatory reaction resulting in the deposition of calcium salts. Such calcification may therefore be evidence of previous or concurrent appendiceal inflammation. The incidence of radiopaque appendiceal fecalithiasis justifies more serious consideration of this entity in the differential roentgen diagnosis of opacities in the right hemi-abdomen. Appendiceal calculi associated with cases of acute appendicitis may frequently present no roentgenological characteristics, considered singly or in aggregate, whereby diagnosis is rendered certain. The clinical picture must be evaluated in interpreting the roentgen findings. Diagnosis of appendiceal calculus may be minimized by the judicious use of supplementary procedures. The most frequent misdiagnosis is right ureteral lithiasis. Definite demonstration of appendiceal calculus in an asymptomatic subject may indicate prophylactic appendectomy. —One case is reported.

Franz J. Lust.

NAKANISHI, K.: *A new type of ameba (ameba ferox) phagocyting pathogen intestinal bacteria, recovered from river water in Java.* Japanese Med. J., 3, 4, Aug. 1950, 231-235.

A new type of ameba, discovered from a river water sample in Java, and measuring 5-28 microns in diameter is described. This organism devours intestinal bacteria, both pathogenic and nonpathogenic. It forms plaque-like figures when planted on the surface culture of susceptible bacteria. It can be maintained in serial subculture when grown with susceptible bacteria on ordinary agar in broth. The name "Ameba ferox" is proposed.

GREENWOOD, J.: *Tumors of the parotid gland.* Texas State J. Med., 47, 4, Apr. 1951, 220-22.

A technique for removal of tumors of the parotid gland, which avoids injury to the facial nerve, is described. Electrical localization and periodic testing of the nerve in this

procedure increases the confidence of the surgeon. In case of damage to the nerve, the technique of repair is offered. As a rule the nerve can be completely spared.

OSBORN, C.: *Cardinoma of the ampulla of Vater.* Med. J. Australia, Apr. 7, 1951, 501-505.

Osborn describes 2 cases of cancer of the ampulla of Vater, the patients having survived the operation of pancreaticoduodenectomy for 3 and 2 years respectively. In diagnosis, the establishment of definite obstructive jaundice is important, pain usually is present, positive benzedrine tests for blood in the stools is suggestive, and enlargement of the gall bladder and liver partially confirmatory. An early diagnosis can usually be made, and radical treatment may be undertaken with a reasonable chance of permanent success. The technical details of the operation are discussed.

BOSSELI, M. A.: *Nephelometric analysis of the euglobulin fractions alpha, beta and gamma of serums in the functional diagnosis of hepatic affections.* Bull. l'ass. d'etudes physio-pathologique du foie et de la nutrition. No. 13, 1950, 86-105.

Flocculation reactions depend on the complex factors regulating the colloidal equilibrium of serums. The euglobulins are the most liable and most susceptible to flocculation in the presence of the various reagents of the tests, of all protein components of the serum. The author presents the techniques used in the nephelometric analysis of the alpha, beta and gamma euglobulin fractions. Results in several cases of liver disease are compared with diagrams obtained by electrophoresis, and a remarkable agreement obtained by the two methods is found. The chief finding in liver disease, where blood protein is altered, is the increase in gamma euglobulin. In pure, parenchymatous disease of the liver there is no increase in gamma euglobulins nor marked flocculation reactions in strong contrast to those cases in which hyperplasia of the fibrous tissues is present. Similarly, there is no augmentation of gamma euglobulin in obstruction jaundice. The analysis of the euglobulin fractions of the serum do not give absolutely specific results, but constitute a great help in the functional diagnosis of a great many hepatic diseases.

BELLEGIE, N. J. AND DAHLIN, D. C.: *Adeno-acanthoma of the stomach, report of 2 cases.* Proc. Staff Meet. Mayo Clinic, Feb. 14, 1951.

Two cases of adeno-acanthoma of the pylorie region of the stomach are reported. A single nodal metastasis of pure squamous-cell cancer was found in one case. This case also had evidence of pancreatic heteropin in the wall of the stomach. Adeno-acanthoma (sometimes called polymorphous epithelioma) is extremely rare in the stomach, only 9 cases having been previously reported. One patient died of wide-spread intra-abdominal metastases. The other patient, operated on in July 1950, is doing well thus far.

INOKI, S., NAGAI, A., KITAMURA, T., TAKADA, S. AND NAKABAYASHI, T.: *Studies on the new culture methods of endomeba histolytica.* Med. J. Osaka University, 2, 2, 53-72, Sept. 1950.

The authors report an improvement on Tanaba-Chiba's medium, replacing Ringer's solution with buffered saline, and replacing the serum with whole blood. Growth was most dense on the third day of culture and maximum growth exceeded that obtained on the Tanaba-Chiba medium by five fold. By a further modification,—replacing the solid portion of the medium with Loeffler's serum medium, maximum growth was obtained in 2 days and was three times as dense as before this modification. Rice flour was found to be indispensable for both formulae.

SALTZSTEIN, H. C.: *Carcinoma of the gastric cardia.* Harper Hosp. Bull., 9, 1, Jan-Feb. 1951.

Cancer of the cardiac end of the stomach is very difficult to diagnose early, so that the outlook has heretofore been practically hopeless. The combined abdomino-thoracic approach now offers a better palliative operation (esophago-jejunal anastomosis by the Roux Y method) and develops a more thorough and radical resection of the primary lymphatic drainage from this area, comparable in completeness to the abdomino-perineal resection for rectal cancer.

W. SANDROWSKI, ST. JOSEFSKRANKENHAUS NIEDERLAHNSTEIN. *On the treatment of ulcus ventriculi et duodeni by 'Cyren'—A implantations.* Med. Welt No. 16, p. 529.

Since August 1947 S. carried out 'Cyren'—A implantations in more than 200 patients for the treatment of ulcus ventriculi et duodeni and other gastric diseases (gastritis, gastroduodenitis, ptosis, cicatrized alterations of the duodenal bulb often accompanied by stenosis and difficulties in evacuation, as well as ectasia and atony) with considerable success. The treated persons comprised men of all age-groups and in single cases women beyond the menopause—young women were given intragluteal injections of 'Cyren'—B crystalline suspensions (5 mg). Favourable clinical results have been achieved with 1 or more 'Cyren' —A implantations in 84% of out-patients and those treated in the clinics.

The results obtained in 75 patients are as follows:

	cases	implantations 1	2	3	4	cured	improved	relapses	surgical intervention	treatment discontinued
gastric ulcer, duodenal ulcer	70	49	16	4	1	49	12	3	3	3
with symptoms of stenosis and atony	5	2	2	1	—	1	1	—	2	2
total	75	51	18	5	1	50	13	3	5	4
%	—	68	24	6.6	1.3	66.6	17.3	4	6.6	5.3

Special advantages of 'Cyren'—A implanations-therapy are abolition of lingering series of injections, of the more or less strict diet, and of confinement to bed, so that the patients can pursue their daily duties.

Clinical cure occurred in most cases after 1 'Cyren' implantation (10 mg). Occasional complaints which mostly set in 3-5 months after the effect of the implantation had faded away, could promptly be removed by a second implantation. Hitherto more than 2-3 implantations have scarcely been necessary.

A special inclination to relapses and remarkable resistance to therapy due to irregular and insufficient nutrition has been observed in motorists, or in patients which were vegetatively stigmatized.

Pains due to swelling of the breasts discontinued within 2-5 days. Besides swelling of the nipples, side-effects (atrophy of the testicles, diminution of potency and libido) were not to be observed.

Franz J. Lust

SCHEINBERG, S. R. AND SALTZSTEIN, H. C.: *Prevention of intra-abdominal adhesions by cortisone and ACTH.* Harper Hosp. Bull., 9, 1, Jan.-Feb. 1951.

While treating a series of Mann-Williams dogs with cortisone, Scheinberg noticed that very few intra-abdominal adhesions developed. Adhesions were then produced in dogs by sprinkling talcum powder along the mesentery and serosa of small bowel (method of Schiff, Goldberg and Necheles). The control animals developed marked adhesions in 14 days but the treated animals showed practically no adhesions. Even 5 mg. ACTH daily was enough to obtain this reult. Authors are now working to determine the dosage which will prevent adhesions without delaying wound healing.

NETZER, S.: *Ten years of pneumoperitoneum.* Am. Rev. Tuberculosis, 63, 1, 62-66, Jan. 1951.

After a ten year experience the author concludes that in patients with predominantly exudative lesions, pneumoperitoneum appears to be beneficial, but it was found to be in unsatisfactory procedure in patients who had the fibrotic type of pulmonary lesions of longer duration

CRUZ, E. AND LEMOS A.: *Human brucellosis in the backlands of the state of Sao Paulo.* Arq. Higiene of Saude Publica, XIII, 35, 75-92, 1948.

From investigations in Sao Manuel, it becomes obvious that human brucellosis has existed since 1941, as well as animal brucellosis. To prevent the diseases spreading throughout Bra-

ail as they have in the U. S. A., the authors recommended intensive studies by veterinarians and physicians.

SCHEINBERG, P.: *Cerebral blood flow and metabolism in pernicious anemia.* Blood, VI, 3, 213-227, March 1951.

Cerebral blood flow and metabolism were studied in 16 patients with pernicious anemia, some having severe anemia and others having moderate anemia or none at all. In the severe group cerebral blood flow was increased and cerebral vascular resistance decreased, while in the other group blood flow was decreased and vascular resistance increased. In both groups, cerebral oxygen and glucose consumption was decreased, as was cerebral venous oxygen tension. There was good correlation between neurological involvement and cerebral oxygen consumption. Even on specific therapy the consumption of oxygen by the brain did not become normal in any instance. Pernicious anemia results in specific nervous system involvement not related to the anemia and this damage is at least partially irreversible in many patients.

STONE, C. T. AND GRATER, W. C.: *Needle biopsy of the liver.* Texas State J. M., 46, 11, Nov. 1950.

From a study of 136 needle biopsies of the liver performed on 82 patients, the authors believe needle biopsy is a relatively safe diagnostic procedure of value, particularly in the study of viral hepatitis. Such studies may eventually clarify the relationship between hepatitis and cirrhosis. There was a general agreement between biopsy sections and the results of function tests, but in some instances biopsy revealed the precise diagnosis when function tests failed to show any abnormality.

BOTHEREAU, N. R.: *Cytologic examination of gastric washings.* Am. Pract. & Dig. Treat., 2, 3, 231-233, Mar. 1951.

The Papanicolaou technique may be employed, using gastric washings which are fixed and stained on a slide, or the residue after centrifuging the washings may be incorporated in a paraffin block, sectioned, stained and examined. Diagnosis of malignant cells requires specialized training. Does the recovery of cancer cells result in an earlier diagnosis than by x-ray and gastroscopy? Do cancer cells desquamate for a long period of time before symptoms and signs appear? It will require ten to twenty years further investigation to answer these important questions.

PETERSON, W. L. AND BASS, L. W.: *Congenital duodenal atresia.* U. S. Armed Forces Med. J., II, 3, 483-489, March 1951.

A case of successful surgical treatment of congenital duodenal atresia in a 6 day old infant is presented. Diagnosis was confirmed by the absence of gas in the intestine on x-ray and by failure of instilled lipiodol to pass the pylorus. This adds one more 6-month survival to the small but growing list of successful cases. Despite prematurity and delay in operation, the condition is not hopeless if good preoperative care is instituted promptly and so long as more serious defects are not present.

GULLICKSON, M. J., SMITH, R. G. AND LARGO, D. J.: *Surgical treatment of gastric ulcer in the aged.* Illinois Med. J., 99, 3, 140-142, March 1951.

Nine cases in whom gastric resection was done because of benign gastric ulcer in persons over seventy years of age, are presented. Only 4 cases presented post-operative complications, viz., disruption of wound, stomal obstruction, pneumonia, and cerebral hemorrhage, there being only one fatality. Strict selection of cases is necessary. The seriousness of gastric ulcer in many aged persons renders radical operation desirable in certain cases in spite of the fact that a higher, though not unreasonable, mortality rate may be met with.

RADKE, R. A.: *Amebiasis with hepatic abscess and pleuropulmonary involvement.* U. S. Armed Forces Med. J., II, 3, 437-444, Mar. 1951.

A soldier with proved hepatic abscess and involvement of the right pleura and lung by ameba histolytica was apparently cured by the use of quinacrine. Carbarsone had no effect on the pulmonary complications.

HALEY, T. J. AND SENNOTT, W. M.: *The diagnostic accuracy of the roentgen examination in diseases of the upper gastro-intestinal tract.* Radiology, 56, 3, 416-419, Mar. 1951.

The results of x-ray examination of the upper gastro-intestinal tract of 202 patients were compared with the surgical findings. In 84 cases of duodenal ulcer the roentgen and surgical findings were in agreement in 88 percent. The roentgen diagnosis was correct in 90.7 percent of 54 vases of gastric ulcer and in 90.7 percent of 33 gastric neoplasms.

BALL, W.: *Roentgen therapy for puritus ani.* Amer. J. Proctology, 1, 3, Sept. 1950, 123-129.

Ball treated 92 persons with puritus ani with radiation. Of these, 90 were idiopathic. 43 cases were completely relieved, 35 partially, and 14 unimproved. The author feels that, on the basis of his experiences, x-ray therapy is definitely indicated in pruritus ani.

KAZMIERSKI, R. H.: *Solitary diverticulitis of the cecum.* Amer. J. Proctology, 1, 3, Sept. 1950, 130-132.

Inflammation of a solitary diverticulum of the cecum is rather rare, only 50 cases having been recorded in the literature. The symptoms are similar to those of acute appendicitis and treatment identical. Frequently on finding the inflamed diverticulum, one tends to regard it as a "second appendix."

HOLINGER, P. A. AND JOHNSTON, K. C.: *Caustic strictures of the esophagus.* Illinois Med. J., 98, 4, Oct. 1950, 246-250.

The authors analyze 96 consecutive cases of caustic burn of the esophagus, showing that the accident usually occurs in children due to the parents having carelessly left a caustic in a glass, cup, coca-cola bottle, etc. Of the cases, 1/3 were acute burns and 2/3 had already developed multiple strictures at the time of the examination. Excellent results have been obtained by beginning dilatation within 24 hours of the accident by means of soft rubber mercury-filled bougies. No strictures have developed in the patients so treated during the 3 years that this regime has been used. In all cases, dilatation in some form must be continued throughout the life of the patient to prevent cicatricial contraction and obviate radical curvative operations.

LITTNER, M.: *Aberrant pancreatic tissue in the first portion of the duodenum.* (Radiology, 55, 5, Nov. 1950, 716-719).

A case is presented in which aberrant pancreatic tissue in the duodenum was erroneously diagnosed as a polyp on the basis of x-ray findings. The occurrence of such tissue in the duodenum is a common finding and results from developmental anomaly. It usually occurs as a single, sessile, intramural nodule of glandular appearance on section. It can be easily confused with ulcer, and may be symptom-producing.

MARTIN, J. F. AND SAUNDERS, H. F.: *Gastric ulcer in childhood.* (Radiology, 55, 5, Nov. 1950, 728-730).

Gastric ulcer in children is rare. A case of acute gastric ulcer with hemorrhage in a child of 6 years of age is reported with x-ray films revealing the lesion. The clinical aspects are similar to gastric ulcer in adults. The patient recovered and the ulcer healed on medical management.

ZINGARO, A. A.: *Pyopneumohepatitis.* (Am. J. Roentg. and Rad. Ther., 64, 5, Nov. 1950).

Pyopneumohepatitis is an abscess of the liver consisting of a cavity containing pus and gas, and presenting the characteristic fluid level appearance. Such a case is described in which an initial diagnosis of gastric cancer with hepatic metastasis was made. Later, a picture of a fluid level in the dome of the liver led to operation in which the pus was successfully evacuated. What had been regarded as a gastric carcinoma was a diverticulum of the jejunum, which may have provided the infective focus for the liver abscess.

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Choosing the best chlorophyll preparation available is of foremost importance if the inherent deodorant properties of chorophyll are to be utilized to their full capacity. Potency, purity, adaptation of the vehicle to the route of administration, and patient acceptance must all be considered as criteria of clinical efficacy. In the development of CHLORESIUM TABLETS all these factors were emphasized. The result is a superior tablet containing chlorophyll in its most active and palatable form.

CHLORESIUM TABLETS contain a greater concentration of highly purified, *water-soluble chlorophyll* derivatives than any preparation now available. Since CHLORESIUM chlorophyll is completely soluble in saliva, it provides more effective local deodorizing action in the mouth. In addition, its solubility in the saliva enables it to reach the intestine in fully active form for systemic deodorization. The saliva acts as a buffering agent to prevent its precipitation and inactivation in the acid medium of the stomach. Tests show that a substantial percentage of chlorophyll contained in other tablets is precipitated and inactivated.

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CHLORESIUM TABLETS have a pleasant, refreshing flavor which permits prolonged retention in the mouth. CHLORESIUM chlorophyll, refined by repeated extractions, is highly purified. The residue of plant waxes and other by-products, inevitably present in any plant extract, has been reduced to an absolute minimum.

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Killian has shown that when gastric acidity is high (pH less than 2) or normal (pH 2 or 3), about 75% of ingested chlorophyll is recoverable from the stomach as a black precipitate. Test tube experiments have demonstrated the effectiveness of saliva in keeping chlorophyll in solution by its buffering action against hydrochloric acid. By increasing the amount of saliva, greater quantities of chlorophyll can be maintained in solution.

Unlike other chlorophyll tablets, which can seldom be retained long in the mouth, CHLORESIUM TABLETS are lozenge-type tablets for slow oral dissolution. This increases the amount of saliva swallowed and ensures buffering of the gastric juice for prevention of precipitation and inactivation of the chlorophyll. In addition, prolonged oral retention of CHLORESIUM TABLETS results in more effective eradication of mouth odors.

GOFMAN TEST AVAILABLE

A new laboratory has been established to widen the availability of the Gofman Lipoprotein Test. This test, developed by Dr. John Gofman and his associates at the Donner Laboratory of the University of California during their studies on atherosclerosis, has been run routinely by the new laboratory for several months on a pilot basis. Ultracentrifugal facilities there are being made available commercially to the medical profession through clinical laboratories.

Blood-serum samples are shipped in special iced containers. By the use of air transportation these tests can be handled from any section of the United States. Results are reported within seven days of arrival of the sample. Price for the test (including transportation costs) has been established at $30. Details of test procedures and significance are listed in descriptive literature available from: Belmont Medical Laboratories, Inc., Belmont 7, California.

FOURTH ANNUAL "RADIATION THERAPY" NUMBER

The November issue of the Mississippi Valley Medical Journal & Radiologic Review (Quincy, Ill.) is the Fourth Annual Radiation therapy contribution by leading specialists. All the papers have been especially written for this number and are designated to appeal to physicians in the general practice of medicine and surgery.

Included in this number are some twenty papers by, J. D. Peak and Marshall Eskridge of Mobile, Ala., F. R. Ruff of Fresno, Cal., M. E. Page of Boulder, Colo., Louis Bernstein of Hartford, Conn., C. W. Perkins of Norwalk, Conn., J. Ernest Breed, I. S. Trostler and Gentz Perry of Chicago, C. R. Drake of Minneapolis, H. R. Schmidt of Winona, Minn., A. J. Delario of Paterson, N. J., C. B. Storch of Brooklyn, J. C. Weisman of Kew Gardens, N. Y., Hirsch Marks and W. L. Palazzo of New York, J. H. Vaughn of Amarillo, Texas, Roy G. Giles of Marlin, Texas, E. P. Mills of Ogden, Utah, H. J. Manning of Elkins, W. Va., and W. L. Waskow of Madison, Wis.

This is the only medical journal publishing a special number in this special field of therapy. It is especially designed to help keep nonradiologists informed of the advances being made in this specialty. The papers are well written and reasonably short and practical, and should arouse in the general profession a greater appreciation of the accomplishments of radiation therapy.

DR. GRAYSON CARROLL, ST. LOUIS, HONORED

Dr. Grayson Carroll, nationally known urologist and teacher of St. Louis University School of Medicine, has been honored by the Mississippi Valley Medical Society as its Distinguished Service Award Recipient for 1951. The award, consisting of a gold medal and a certificate, was presented to Dr. Carroll at the banquet on the occasion of the 16th Annual Meeting of the Society at the Pere Marquette Hotel, Peoria, Ill., Sept. 20. Dr. Carroll is Assoc. Prof. of Urology, St. Louis University, Head of the Dept. of Urology at St. Louis City Hospital and was President of the Mississippi Valley Medical Society in 1946.

Each year the Mississippi Valley Medical Society presents a Distinguished Service Award to one of its members "who has rendered unusual and distinguished service to the medical profession." Members who have received this award in previous years include: Dr. Vilray P. Blair, Prof. Emeritus of Clinical Surgery, Washington; Dr. Alphonse McMahon, Associate Prof. of Medicine, St. Louis University; the late Dr. Joseph B. DeLee, Prof. of Obstetrics, University of Chicago; Dr. Nathaniel G. Alcock, former Prof. and Head of the Dept. of Urology, University of Iowa; Dr. Frederick H. Falls, Prof. and Head of Dept. of Obstetrics and Gyne-

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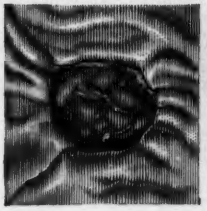

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RESINAT, the original medical application of anion exchange resins in the treatment of peptic ulcer, is now available in plain tablet form. Correct dosage. Quicker disintegration. Faster action.

How Supplied: Plain Tablets each 0.5 Gm. In bottles of 36, 100, and 1000.

Also available in Capsules (0.25 Gm.), Sugar-coated Tablets (0.5 Gm.), Powder (1 Gm.).

RESINAT brand of polyamine-methylene resin for peptic ulcer

Literature and samples on request

The National Drug Company
Philadelphia 44, Pa.

more than half a century of service to the medical profession

the NEW therapy in "functional G. I. distress"...

Decholin with Belladonna

Patients complaining of gastrointestinal distress without detectable organic cause are common problems in daily practice. By combining spasmolytic action with improvement in liver function, *Decholin/Belladonna* – in such cases – gives symptomatic relief by

reliable spasmolysis

hydrocholeretic flushing of biliary tract

improved blood supply to liver

mild, natural laxation without catharsis

While of special value in functional dyspepsia, *Decholin/Belladonna* is, of course, treatment of choice in biliary tract disorders for thorough and unimpeded flushing of the biliary system.

DOSAGE: One or, if necessary, two *Decholin/Belladonna* tablets three times daily after meals.

PACKAGING: *Decholin* (brand of dehydrocholic acid) *with Belladonna*, bottles of 100 tablets. Each tablet contains dehydrocholic acid 3¾ gr. and belladonna ⅛ gr. (equivalent to tincture of belladonna, 7 minims).

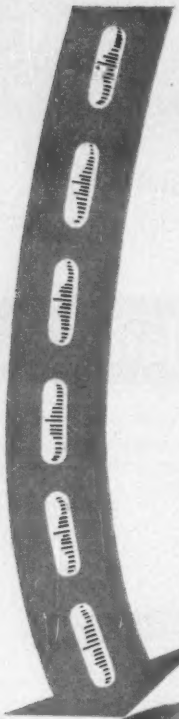
Decholin, trademark reg.

AMES

AMES COMPANY, INC., ELKHART, INDIANA

AMES COMPANY OF CANADA, LTD., TORONTO

DB-1p



DIAGNOSIS CAN BE DEFINITE!

because...

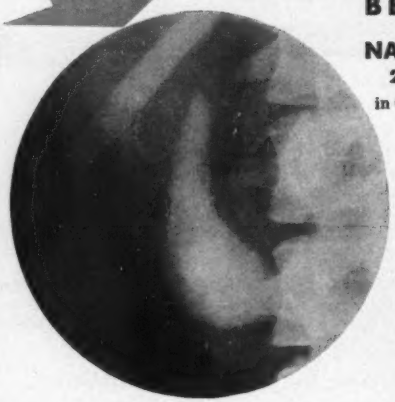
1. **MONOPHEN** "normals" are consistently sharp and clear.
2. Diseased gallbladders visualize poorly or not at all.
3. This diagnostic trustworthiness has been attested to by its use in over 3000 cases . . . *with complete confirmation of those cases where surgical intervention was recommended.*

In addition, the proven infrequency of side reactions such as cramps, diarrhea, dysuria and nausea, makes the easily swallowed **MONOPHEN** capsules ideally suited for routine use, particularly since double doses are unnecessary.

Wasch, Milton G. and Epstein, Bernard S.: Am. J. Roentgenol. & Rad. Ther., 66:96-102, 1951. MONOPHEN—A New Medium for Cholecystography.

Epstein, B. S., Natelson, S. and Kramer, B.: Am. J. Roentgenol. & Rad. Ther., 56:201-207, 1946.

MONOPHEN
THE MODERN CHOLECYSTOPAQUE



BELL-CRAIG, INC.
formerly
NATIONAL SYNTHETICS, INC.
270 Lafayette Street, New York 12
in Canada: 270 Parliament St., Toronto 2

"Dependability Through the Years"

WHY DON'T YOU TRY MONOPHEN?

MONOPHEN is 2-(4-hydroxy-3, 5-diiodobenzyl)-cyclohexane carboxylic acid, containing 52.2% iodine in stable combination.

SUPPLIED IN BULK: Capsules (0.5 gram) are cellophane-sealed and boxed in quantities of 50, 100, 250, 500 and 1000 with a requisite number of dispensing envelopes imprinted with directions for use.

Write for samples

in peptic ulcer–

NEW CONVENIENT CHLOROPHYLL THERAPY

Chloresium MUCINOID Tablets • Powder

for rapid relief of symptoms and tissue repair even in intractable cases

All the advantages of CHLORESIUM POWDER* are now available in convenient *tablet* form: same unique combination of healing agent plus antacids in a mucin-like base — same superior clinical results — and in a form that's easy to take.

highly concentrated, purified water-soluble chlorophyll promotes healing of affected areas, duplicating the outstanding results obtained in treatment of external lesions.

specially prepared, mucilaginous okra base clings tenaciously to mucosal walls, protecting against erosion and maintaining the chlorophyll in prolonged contact with the lesion.

prompt, sustained antacid action — without undesirable side effects — provided by magnesium trisilicate and aluminum hydroxide.

packaging: CHLORESIUM MUCINOID is available in bottles of 50 and 200 tablets and in boxes of 25 powders.*

*CHLORESIUM POWDER will continue to be available in boxes of 25 envelopes but will now be sold under the name CHLORESIUM MUCINOID.

RYSTAN COMPANY, INC. Mount Vernon, N. Y.

Wyeth®

In Peptic Ulcer

"The initiation of a healing reaction in the lesion is the surest safeguard against further bleeding"[1]

When therapeutic response must be prompt—the double gel action of Amphojel provides:

- Rapid lowering of gastric acidity to noncorrosive levels
- Protective coating of the exposed lesion to facilitate healing
- Quick relief of ulcer pain with subsequent release of mental and physical tension

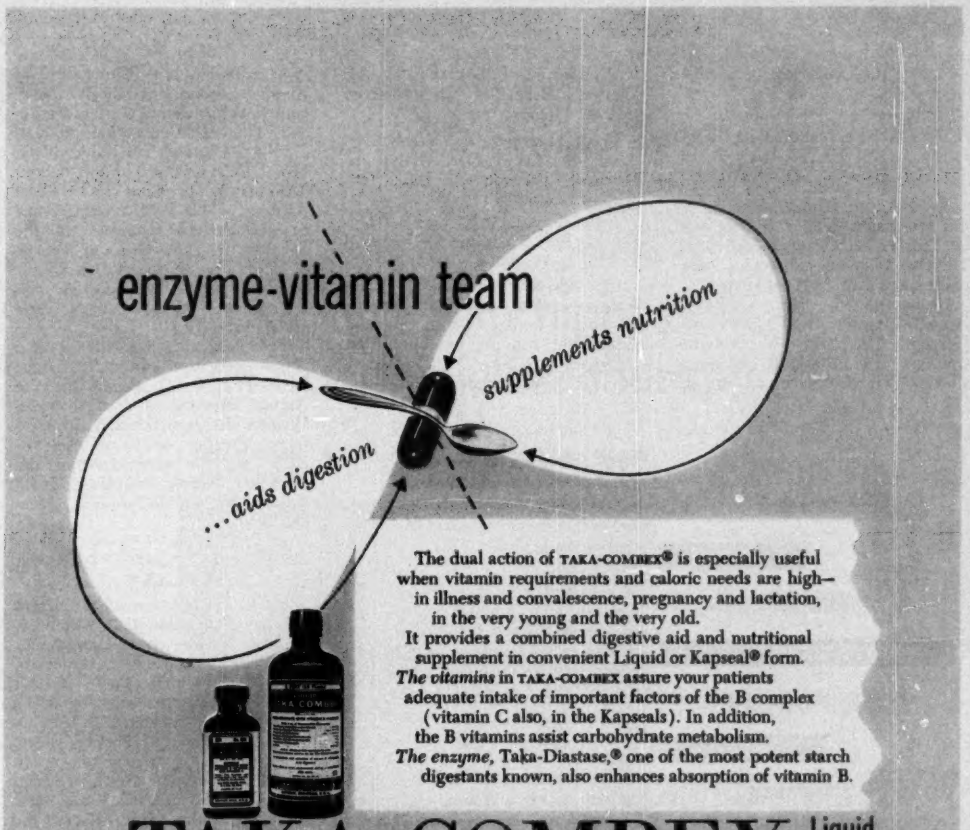
AMPHOJEL®

ALUMINUM HYDROXIDE GEL
ALUMINA GEL WYETH

Pleasant tasting . . . Economical
Available in bottles of 12 fl. oz.

1. Larimore, J. W.: Southern M. J. *44*:742, 1951.

Wyeth Incorporated, Philadelphia 2, Pa.



The dual action of TAKA-COMBEX® is especially useful when vitamin requirements and caloric needs are high—in illness and convalescence, pregnancy and lactation, in the very young and the very old.

It provides a combined digestive aid and nutritional supplement in convenient Liquid or Kapseal® form.

The vitamins in TAKA-COMBEX assure your patients adequate intake of important factors of the B complex (vitamin C also, in the Kapseals). In addition, the B vitamins assist carbohydrate metabolism.

The enzyme, Taka-Diastase,® one of the most potent starch digestants known, also enhances absorption of vitamin B.

TAKA-COMBEX Liquid Kapseals

TAKA-COMBEX Kapseals

Each Kapseal contains:

Taka-Diastase (*Aspergillus oryzae* enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	10 mg.
Vitamin B_2 (Riboflavin)	10 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (Sodium Salt)	3 mg.
Nicotinamide (Niacinamide)	10 mg.
Vitamin C (Ascorbic Acid)	30 mg.

With other components of the Vitamin B Complex derived from liver.
In bottles of 100 and 1000.

TAKA-COMBEX Liquid

Each teaspoonful (4 cc.) contains:

Taka-Diastase (*Aspergillus oryzae* enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	2 mg.
Vitamin B_2 (Riboflavin)	1 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (As the Sodium Salt)	2 mg.
Nicotinamide (Niacinamide)	5 mg.

In 16 ounce bottles.

PARKE, DAVIS & COMPANY

MEDICAMENTA VERA

cology of the University of Illinois; etc.

NEW DIRECTORS ELECTED TO MISSISSIPPI VALLEY MEDICAL SOCIETY

At the 16th Annual Meeting of the Mississippi Valley Society held in Peoria, Ill., September 19, 20, 21, the following directors were elected to serve for two years:

From Illinois: Dr. Norris J. Heckel, Chicago; Dr. F. Lee Stone, Chicago; Dr. Arkell M. Vaughn, Chicago; Dr. Pliny R. Blodgett, Chicago Heights; Dr. George E. Kirby, Spring Valley; Dr. W. H. Walton, Belleville; Dr. Warren Pearce, Quincy.

From Missouri: Dr. Wendell G. Scott, St. Louis; Dr. Arthur S Bristow, Princeton; Dr. Julius Jensen, St. Louis.

From Iowa: Dr. George C. McGinnis, Fort Madison; Dr. Edward L. Rohlf, Waterloo.

The Scientific Exhibits at Peoria were excellent and the Awards Committee had a difficult time deciding the winning exhibits. First Prize went to Drs. A. S. Gordon, Max Sadove, Frank Raymon and A. C. Ivy of the University of Illinois; Second Prize to Dr. Cleveland J. White of Loyola University, and Honorable Mention to Dr Carroll P. Hungate of Kansas City, Mo., for his elaborate exhibit "Atomic Energy and Its Medical Aspects." The 1951 Distinguished Service Award Recipient of the Society was Dr. Grayson Carroll of St. Louis University. No Honor Award or prizes in connection with the Annual Essay Contest were given this year.

The 1952 meeting will be held at the Jefferson Hotel, St. Louis, October 1, 2, 3, during the 9th Annual Meeting of the American Writers' Ass'n, which will also meet there. Further details of the Society may be secured from the Secretary, Harold Swanberg, M. D., 209-224 W. C. U. Building, Quincy, Ill.

CANCO EXPANDS ST. PAUL PLANT

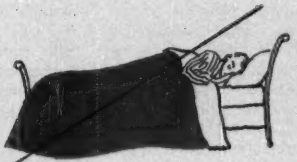
Virtual completion of a current expansion program that will nearly double the annual container manufacturing capacity at American Can Company's St. Paul (Minn.) plant has been announced by A. C. Hubbell, plant manager.

Several new production lines, each capable of turning out up to 400 cans per minute, have been installed, Mr. Hubbell said, and the plant is now ready to serve the growing demands for containers by vegetable canners and meat packers in the greater Twin Cities area. The expansion also will mean a marked increase in the plant's personnel, he said.

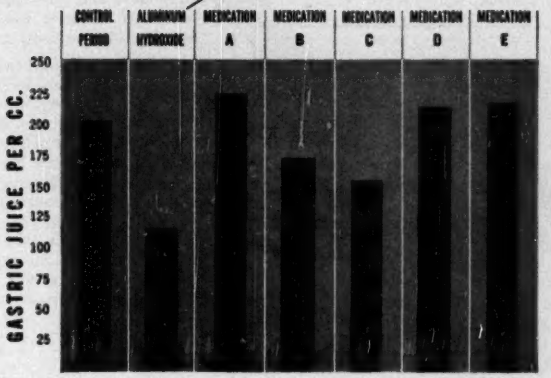
The Canco plant manager pointed out that there has been an 83 per cent gain in acreage for the leading vegetable packs in the states of Minnesota and Wisconsin over the last 17 years. By providing a greater supply of locally produced metal containers, he said, the can company will be able to meet the seasonal demands of customer industries and satisfy requirements for a greater variety of cans.

Although Canco's St. Paul plant in the past has manufactured containers mainly for ham, lard, cream and eggs, the new expansion will enable it to produce millions of vegetable and key-opening meat cans annually, according to the plant manager.

The new additional manufacturing facilities are housed in a one-story



No waking with night pain on this ulcer therapy



Average volume of gastric secretion from midnight to 5:30 A.M. in patients with duodenal ulcer treated with various medications *during the day only*. Aluminum hydroxide depresses volume of gastric secretion more effectively throughout entire night period. (Adapted from Brehaus, H. C., Akre, O. H., and Eyerly, J. B.: *Gastroenterology*, 16:172, Sept., 1950.)

By taking Creamalin *during the day only*, the peptic ulcer patient will sleep undisturbed from midnight to morn.

No waking by the alarm clock for medication. Creamalin taken only *during the day and evening* acts all night to produce a marked reduction in gastric secretion.

No waking with night pain. Creamalin is amorphous, acid-soluble reactive, aluminum hydroxide, the most efficient of the alumina gels for prompt and prolonged buffering of acidity.

Creamalin®

(amorphous, acid-soluble, reactive aluminum hydroxide gel)

Winthrop-Stearns INC.

NEW YORK, N. Y. • WINDSOR, ONT

Creamalin, trademark reg. U. S. & Canada

structural steel and brick building, containing approximately 74,000 feet of floor space, adjacent to the existing plant. The production equipment, Mr. Hubbell said, is of the most modern design and includes facilities for applying protective coatings on the cans as well as coating ovens, bodymakers, flangers and advanced testing apparatus. The building contains spacious storage areas and is provided with improved truck and car loading spots.

Completion of the plant expansion this year is of dual significance, said Mr. Hubbell, in that it makes St. Paul one of the most modern can manufacturing centers in the country and marks the can company's 50th anniversary in Minnesota, dating back to the turn of the century when the company was formed.

The history of Canco's plant in St. Paul, however, goes back to 1879. At that time the small firm of Horne and Danz began manufacturing some metalware, which included patent folding decoys for ducks and geese. It was not until that firm became part of the American Can Company that periodic expansions took place which have brought it to its present capacity.

Canco's half-century of operation has marked the development of many can-making techniques of importance both to the canning industry, and consumer, according to Mr. Hubbell. Among the foremost of these contributions, developed in Canco laboratories, was the perfection of the modern open-top can as compared with the old "hole-in-top" can in use at the turn of the century, he explained, pointing out that this development greatly expanded popularity of canned foods. This advance also opened the way for fully automatic manufacturing methods, which eliminated the slow and expensive procedure formerly used in turning out the old type cans.

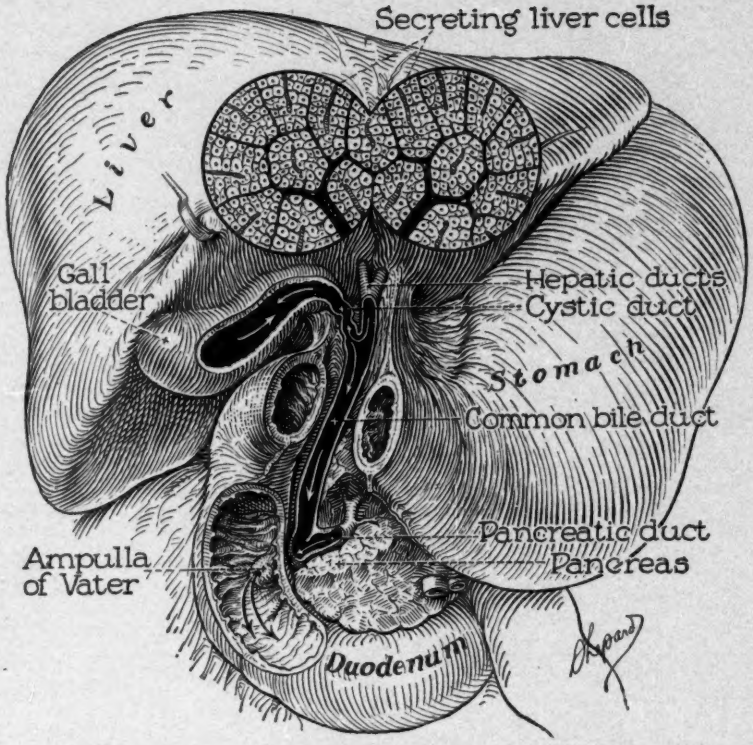
The enlarged facilities of the St. Paul plant are considered by the can company as among the best of the 60 can-making factories and machine shops operated by the company in the United States, Hawaii and Canada. In planning the current expansion, the American Can Company has made provision for future plant growth in St. Paul, if required, to keep pace with the growing needs of the agricultural and canning industries throughout the greater Twin Cities area.

INDEX TO ADVERTISERS

The only broad-spectrum antibiotic available in concentrated drop-dose potency, Crystalline Terramycin Hydrochloride Oral Drops provide 200 mg. per cc.; 50 mg. in each 9 drops. Indicated in a wide range of infectious diseases, Terramycin Oral Drops are miscible with most foods, milk and fruit juices, affording optimal ease and simplicity in administration.

Supplied | *2.0 Gm. with 10 cc. of diluent, and calibrated dropper.*

ANTIBIOTIC DIVISION **Pfizer** CHAS. PFIZER & CO., INC., *Brooklyn 6, N. Y.*



The medical management of gallbladder disease is a physiologic approach to improve hepatic function and to alleviate biliary stasis. The rational regimen of therapy includes:

1. Adjusted diet containing uncooked fats, as tolerated, which induce emptying of the gallbladder.
2. Ketocholanic acids—**KETOCHOL**®*—to stimulate the flow of bile and "flush out" the biliary tract.
3. Antispasmodic medication—**PAVATRINE**® with Phenobarbital**—to relax the sphincter of Oddi and allay irritability of the gastrointestinal tract.

*Ketochol combines all four of the oxidized form of the normal bile acids.

**Pavatrine with Phenobarbital combines the smooth muscle relaxant, Pavatrine, with phenobarbital.

SEARLE RESEARCH IN THE SERVICE OF MEDICINE

NOVEMBER, 1951 THE AMERICAN JOURNAL OF DIGESTIVE DISEASES PAGES 323 TO 338 VOLUME 18, NUMBER 11